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FROM

The Editors

10 Jan., 1887 – 23 Apr., 1892

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viii 304

VOL. III. No. 1.

AN
EPHEMERIS
OF
MATERIA MEDICA, PHARMACY,
THERAPEUTICS
AND
COLLATERAL INFORMATION.

JANUARY, 1887.

BY

EDWARD R. SQUIBB, M. D.
EDWARD H. SQUIBB, S. B., M. D.
CHARLES F. SQUIBB, A. B.

BROOKLYN, N. Y.
1887.

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NOTICE.

The number of applications for these pamphlets has been unexpectedly large, and most persons have wanted the back numbers; many also have lost back numbers who wanted to file them, and have had to write for duplicates. Some at first were supplied free of cost, but several numbers of each volume have had to be reprinted at considerable additional expense, and therefore all future applicants will be asked to pay for them.

Because of the time and postage required in answering letters, neither the pamphlets, nor a reply and explanation need be expected unless the price of the numbers desired be sent with the application for them.

For each back number desired the sum of ten cents must be remitted with the application, in postage stamps or by postal note, this sum covering the cost and postage on each number applied for.

The two complete volumes are now accessible to all those who want them, bound separately in cloth. They will be sent free of postage for $1.16 each.

AN EPHEMERIS

OF

MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

VOL. III. JANUARY, 1887. No. 1.

A year ago the issuing of these pamphlets was abandoned with regret, and as inclination and material are not wanting, they would be gladly resumed with something like the original frequency, if only the time for the necessary work was at command. Experience has shown that it is one thing to know a subject fairly well in a general way, and even to practice upon it with success, but quite another thing to write upon it with that degree of accuracy and definiteness necessary to publication for the use and information of others. As a rule, the work has to be done at or near the time when it is to be described, and in a busy life, with occupations hourly changing, special attention to one subject is at best confused and disturbed, and in a little while details get crowded out and forgotten. The one condition essential to successful work for publication seems to be abstraction from other occupations for a few hours at a time at least, and this the writer can very rarely command now that age and failing faculties have made night work impracticable.

Under these circumstances, all that is indicated by the issuing of this pamphlet, as a number of the former series whereby a third volume is begun, is that as time and circumstances may permit, it is proposed to prepare some material for publication, and whenever such material may be in readiness, to offer it in this form, even if that should only be once or twice in a year.

The writer has many papers which are occasionally asked for, published during the past thirty years in books not accessible to all interested in these subjects. Some of these, at least, he would very much like to revise and republish in this form if it were reasonable to entertain a wish so unlikely to be accomplished.

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MEDICINE AND PHARMACY ABROAD.*

In the course of an European excursion of nearly eight months' duration, the writer gave a good deal of superficial, general attention to what could be seen without special investigation, of the condition of the arts of medicine and pharmacy abroad, as compared with what might be seen by a traveler under similar circumstances in this country, and the results may possibly be worth recording.

The observations embraced many of the principal cities of Europe from Trondhjem at the north to Naples at the south and Moscow at the east, and included in the order in which they were visited Ireland, Scotland, England, Denmark, Norway, Sweden, Finland, Russia, Germany, Austria, Italy, Switzerland, France, Holland and Belguim.

In order to give an idea of the looseness and inaccuracy with which the observations were made, it must be stated that in visiting one or more of the principal cities of these nations it was a prominent object to see as much as possible of the outlying streets, and the people who inhabited them, and in noticing their shops and their occupations, to compare these with each other and with the cosmopolitan character of the principal or central streets, which latter are much alike in all the large cities. For example, it was very interesting to notice the number of, and the proportion between, the butcher, baker and vegetable markets and shops, in one group,—the fruit and flower shops for another group,—the tobacco, beer, wine and candy shops for another group,—and so on,—and, as being of especial interest, the number of doctors' signs, and of pharmacies.

In passing it may be noticed that the principal streets, and the principal hotels and their inhabitants in all the very large cities are not only much alike in appearance, but, probably from being in the direct line of such an enormous amount of travel, they are really cosmopolitan, having lost much of their nationality, and become in one sense international, especially in the dress, manners and language of the people. The French, English and German languages are so common in these special localities as to approach universality, so that no traveler having any one of the three is ever long at any great disadvantage. In the hotels and principal shops especially, these languages are very common, and in the porter's lodge or breakfast room one would hardly know whether he was in Trondhjem, St. Petersburg, Venice or Naples. But often so near as within two or three streets of these centres of intermingled nationality, localities are reached which offer a striking contrast of special nationality; but the contrast is in faces, habits, manners and language of the people and in their houses and shops, rather than in dress. The distinguishing nationality of costume is rapidly disappearing everywhere, and is hardly noticeable in many of the cities, so that the clothing stores throughout civilized Europe appear to be more nearly alike than those of any other merchandise.

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* Read at the Third Annual Meeting of the New York State Medical Association, held in New York city, November 16th, 1886.

As a broad generalization, there seemed to be fewer butcher shops, more bakeries and vegetable shops and markets,—more fruit and flower shops;—fewer wine and beer shops and much fewer candy shops, than in this country.

But in the special interest of medicine and pharmacy, the contrast was far greater than in anything else. In all the nations of civilized Europe this interest is recognized as being of superior importance, and is under more or less of legal and moral restraint and control. In no nation,—not even Great Britain,—is this interest so nearly a free trade as in this country. The theory is that all governments,—that of this country included,—have laws for the protection of the people against the pretensions and deceptions of quackery, and deficient knowledge and skill, in the important art of medicine, but certainly in no nation has this art become debased so nearly to the level of the money-making trades as in this country; and Great Britain seems to rank next in this unenviable debasement, while Denmark and Sweden seem really to have the interest under the best practical control. Not that the science of medicine is as advanced in these nations as in Germany, for example, nor the art practiced with so high a degree of knowledge and skill as in England and this country, but it is simply under better control, and therefore the people's interests in it are better protected.

In counting the physicians' offices in the large European cities, and trying to compare the numbers with those of Boston, New York, Philadelphia and Baltimore, it seemed to the writer that in the latter cities the numbers were more than double. In the European cities street after street of those occupied as residences would be traversed with but one or two doctors' signs,—or with none at all. And among the few signs the number of comparatively new ones was very small indeed. From occasional glimpses into these offices,—or at least into the front rooms, through open windows, they were judged to be very plainly furnished,—hardly what would be called comfortable, and never luxurious, whilst the absence of any degree of ostentatious display marked the infrequency of the quackish class. The number of physicians' vehicles that could be in any way identified as such, in the streets during the customary hours for visits, was so small that a pretty close scrutiny was needed to find them at all. Indeed, the conclusion was reached that in those cities physicians must generally walk or use public conveyances, and this conclusion was strengthened by seeing that visits to patients at hotels were commonly made on foot.

There is no such thing as recognizing these physicians as a professional class, and the very few seen that were identified by circumstances were very plain and simple in dress and manner, and in dignity of bearing hardly supported the importance of the profession. Some indication of their popularity as a class, or of the general impression of their utility to the public, was sought for in vain; nor was it practicable to ascertain how far their counsels extended among the masses,—how far they were accepted,—or how far their instructions were carried out, but from slight indications it is supposed that their standing and influence is greater than in this country. And this should be true if for no other reason than that their art is practically free from the debasing competition of advertising quackery and nostrums.

The pharmacies of European cities offer a much more striking contrast to those of this country. In England and Ireland they appear to be similar in character, but perceptibly less numerous. In Scotland they are less conspicuous and less numerous than in England, and in France the character and number are still further modified for the better. But it is in other European cities that the contrast becomes most marked. As a broad generalization it may be that in number they reach one-third of the number in this country, but probably not over one-fourth; but the contrast in character and appearance is still more remarkable than in number. Never near together they are commonly in prominent locations, and not uncommonly appear to occupy the whole of a small building. No show window nor colored bottles nor any other form of display. Windows of ordinary size and character, and used only to admit light, except that they may occasionally have one or two growing medicinal plants. No glaring nor large signs anywhere, but generally a small one over the entrance door with the name of the proprietor, and the word "Apotheke." Inside the door is a clean clear space occupied by a few chairs. Then a very simple counter without show cases, and without furniture, or with one or two scales of large size. Behind the counter and with their backs toward it are from one to four clerks, each with a prescription scale and measures, engaged in putting up prescriptions or orders. Beside these, the proprietor or his representative appears to be engaged in receiving those who enter, and in superintending the work of the clerks. As a general rule males who enter remove their hats as soon as the door is passed, and remain uncovered until they are served and go out. In many visits to such pharmacies very few verbal messages were noticed, almost all messengers bringing written orders or prescriptions, though they often received only a single article. The proprietor or disengaged clerk receives the order, and invites the bearer of it to sit down, and not once was a messenger seen to sit down without being invited. Often not a word was spoken until the order was supplied and presented, when the clerk would mention the price, or the messenger would ask for it, and as a rule conversation seemed to be avoided. The clerks were generally of mature age, intelligent looking, personally clean and well, though very plainly dressed. The furniture and apparatus was clean and in good order, but clumsy, and there was a notable absence of gaudy overgilt labels and ostentatious decoration of anything, everything being plain and substantial, even to ugliness and clumsiness. Not a patent medicine card, nor any proprietary article in sight, and no perfumery, fancy goods, soaps, cigars, wines, waters, nor soda fountain in sight. In short, the whole pervading tone was of quiet, earnest and accurate work of a high order, carefully done, and this tone gave a dignity and an honorable rank to the whole place. The writer commonly made an errand of buying a few grammes each of ether, chloroform and carbolic acid, articles the quality of which could be fairly judged by their sensible properties, and such purchases gave access to the pharmacies, and opportunity to observe the work. The first of these orders was given in Copenhagen verbally through a clumsy mixture of bad French and worse Latin. The clerk, a very young man, very respectfully suggested English, in an excellent specimen of that tongue, and never after was the writer again caught in the same way, and this led to the observation that, with very few exceptions, English was spoken and understood in the pharmacies of Europe.

The articles bought were often of very good quality, and never of bad quality, and were uniformly dispensed quickly and neatly, but never elegantly.

The general conclusions reached by these observations were, that in the United States there is a class of physicians who, in ability, knowledge and skill in the application of their art, are not excelled by any similar class in Europe, but that in this country this class is so diluted and obscured by the much larger class with superior pretensions and inferior knowledge and skill, who keep themselves so prominently before the public as to overshadow the better class and give a superficial appearance of inferiority to the profession as a whole.

By the uncontrolled multiplication of graduates of medicine here, the profession is overcrowded with indifferently educated men far beyond the demand or necessity for their services, and far beyond the proportionate number in any other nation. If this struggling surplusage and its influences be subtracted, the profession of medicine in this country is probably nowhere excelled.

The condition of pharmacy in the United States appears to be fairly parallel to that of medicine. In no country are there any better medical supplies than in this, and in none are these better managed and dispensed for use than in this. Indeed, with respect to both quality and management, there is a strong probability that there is a superiority here. But, there is certainly no country more abundantly supplied with bad drugs, nor with the ability and skill to put them in the place of good ones. In most European countries pharmacy is so controlled that it is not very easy to get bad medical supplies, while in this country, with pharmacy almost uncontrolled, it seems not very easy to get good ones. With good and bad material in equal abundance, the pharmaceutical ability and skill which constitutes good pharmacy in the one case makes very bad pharmacy in the other, and against this last the European control measurably protects European physicians and their patients. Here there is probably better pharmacy and more of it than there; but here there is an enormous amount of bad pharmacy to contrast with a very little there.

THE RELATIONS OF PHYSICIANS TO THEIR MEDICAL SUPPLIES.*

There are a large number of physicians who, for both therapeutics and materia medica, depend largely,—if not mainly, —upon the traveling salesmen and their pamphlets and lists, and on the advertising pages of the medical journals. The relations of this class to their supplies is most simple and most favorable. They come in very direct and very close contact with the sources of their supplies, and have much less trouble than any other class of artisans. With others smarter, more ingenious and more plausible than they, to think for them, and then to apply vigorous mercantile principles to their wants thus suggested for them, they have the least practicable amount of thinking for themselves to do, in regard to their remedies and the novelties of the day, and therefore, as they argue, more time to think of and study out their cases. To this class the ready-made prescriptions in the form of beautifully colored and coated pills, or palatable solutions and mixtures, do not appeal simply as gratifying various degrees of laziness, or indisposition to think for themselves, but they present themselves as true labor-saving devices, skilfully prepared for the over-worked ability to use them, and as giving more time for the higher and more scientific reaches of the profession. Perfunctory routine in the observation of cases soon leads to a routine practice of treatment, and then what can be more convenient or more desirable than ready-made supplies in an attractive form, easily accessible. For example, the fashionable "nervous prostration" being observed, what can be more simple or more easy than to order Smith's "coated pills of Valerian, Quinine, Iron and Zinc, No. 1," to be taken three times a day, and a draught of Jones' Effervescent Salts of Bromide of Potassium, Caffeine and Cocaine in solution at bed time. There are few difficulties in this practice of medicine and none in the way of medical supplies, for the physician himself may easily have a supply of the medicines at 10 per cent. off from "list prices," or may send for them to the nearest town or village, where a pharmacist or a general store will have them at a cost of 25 per cent. off from "list prices." But, should the traveling salesman for that district have been a fifteen hundred dollars a year man, instead of a man at three thousand dollars, he may not have succeeded in leaving the articles in that town or village. Then, in 24 hours, by telegraph and express, they can be obtained from the nearest wholesale druggist or jobber, who buys them of the manufacturers at 10 per cent. less than the 25 per cent. off price of the town or village dealer. Whether this last 10 per cent. discount is really "the bottom" few people know, but probably it is not.

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* Read at the Third Annual Meeting of the New York State Medical Association, held in New York city, November 16th, 1886.

If the patient sees that Smith's pills "worked well," he might want them again, or recommend them to his neighbors. In such a contingency the physician would be likely to be avoided. Unless he had successfully secreted the name of the pill, the patient or neighbor would go directly to the store with the pill box, or its number and date, and would buy his medicine at say "list price." The physician gets 10 per cent. below this. The pharmacist or storekeeper gets 15 per cent. below the physician or 25 per cent. below the consumer. The wholesale druggist or jobber gets 10 per cent. below the pharmacist, or 32.5 per cent. below the consumer, so that if there should be no other discount below this, the manufacturer realizes for his wares 67.5 per cent. of his list prices, or 32.5 per cent. below what the consumer pays; and as the manufacturers' profit should not be less than 15 per cent upon what he realizes for his supplies, this brings the net cost of his products to him, at about 57.4 per cent. of what the consumer has to pay for them if he pays "list prices." These are all just and fair profits. Not at all greater than is right and expedient and necessary to the transaction of a fair and honest business if such business is to be moderately successful, and pay as many middle men. These middle men are the so-called distributors in the economy of trade, and are considered indispensable between the manufacturers and consumers.

Although there is probably a very large amount of this business done at about these figures, the constantly increasing number of manufacturers and specialties, and the intense competition in trade, all the way along the line from the consumer to the base of supply, introduces a great deal of what is called "under-cutting" prices. The town pharmacist to attract patronage away from his competing neighbors will often reduce his profits by offering to retail at prices 5, 10 or 15 per cent. below "list prices," and to attract physicians to his pharmacy may offer to double their 10 per cent. profit upon what they want. Such pharmacists are reproached with being "cutters," and when attempts are made to coërce them back into the ranks, or to boycott them, they take up the defence of advertising themselves as "cutters" to attract buyers at low prices.

Then if they sell double the quantity in a given time at half the uncut profits, they are as well off as those who sold half the quantity in the same time at the fair normal profit intended by the manufacturer in his scheme of discounts.

The objects of this recital are to show that there is but little difficulty or obstruction in the relations of this class of physicians to their medical supplies; and that the principal reason of this great success is that every one along the whole line of trade, from the manufacturer to the physician and patient, makes a fair money profit out of the business; and then to bring into contrast with this condition of things, other conditions which co-exist in the common markets for medical supplies.

There is another class of physicians who are independent of the traveling salesman and of the advertising pages of their journals; who do more of their own thinking, and who find time not only to study out their cases but also to give equal attention to the selection and adjustment of their remedies to the individual cases. Through habits of close and well trained observation they acquire ability to know whose testimony to take in aid or correction of their own experience, and ability to know whom to distrust.

With the progress of their art, their therapeutics and materia medica become more simple yet more vigorously applied. They want few combinations suggested to them, but rather want each individual case to suggest such combinations as may be indicated by symptoms which may vary from hour to hour, or day to day. To many physicians of this class complex prescriptions and combinations are very infrequently used. If in any case there should be distinct indications for more than one therapeutic effect, the agents required for such effects are used not together, but alternately, thus avoiding the risks of both chemical and physiological incompatibility and allowing the doses to be varied with the increase or decrease of the separate indications.

In all such practice each agent of the materia medica acquires its maximum importance; and as an indispensable condition to maximum importance it must be of standard quality. The standard of quality for the accepted and established agents of the materia medica is the Pharmacopœia, and this class of physicians rarely go beyond its scope, unless it be upon satisfactory evidence that some new agent may better fulfill their indications than the old ones. And in this connection it may be said that very many of this class are wisely cautious and suspicious of novelties, first because it is impossible to discriminate between those which are of the catchpenny order and those which are not; and secondly, because novelties in their most attractive period have no standard of identity or quality.*

Now, what are the relations of this class of physicians to their kind of medical supplies?

The physicians and patients who want the highest attainable quality and least complexity in medical supplies, and who apply ordinary common sense to know when they get them, may not be in largest number, but yet they are sufficiently numerous to create an active, earnest and large demand, and this by the laws of trade should be met with a plentiful supply; and the demand is thus met, for there is always an abundant supply of excellent medicines in all the mercantile centres of trade, But away from the central markets they are not equally accessible; and in pretty accurate proportion to the distance from the central markets the difficulty of obtaining them is increased. The statement that there is at all times an abundant stock of good medical supplies at a few of the principal commercial centres, and that such become more and more scarce in proportion to the distance from these centres, will hardly be questioned; and if true this indicates very clearly that the difficulty of access to this stock is simply a difficulty of distribution. This is equivalent to saying that the distributors or middle men,—namely, the wholesale dealers and jobbers throughout the country, and the brokers and agents who represent them in the few principal commercial centres, do not favor the distribution of this class of supplies. Then comes the question, why they do not favor this class of supplies and distribute them as freely as they do other kinds, since, everything else being equal, all dealers, from first to last, will always prefer to deal in good articles, and as a rule have knowledge enough to discriminate between the good and the bad.

The answer to this must be somewhat as follows:

Briefly stated, it is because they are not permitted to make as much money on good as on inferior supplies; and the good are disfavored because they offer a standard for comparison or contrast with the inferior in quality, which tends to throw a distrust upon the latter class that would not be felt in the absence of a standard class.

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*A single retrospect will serve to emphasize and justify this caution. Not less than five different substances were sold as Chian Turpentine, and some of the strongest cases of the many published cures must have been treated with clumsy imitations.

The merchant, as such, follows his business to make money by it, and the dealers in medicines are no exception to the rule. Medical supplies to them are simply merchandise, and are dealt in very much as railroad supplies, groceries and dry goods are, and the invariable and inevitable law of trade is to favor the articles upon which most money is to be made. In conformity to this law of trade, if most money could be made off of the best goods, then the best would always lead in all markets—not only at the centres, but also down the whole line of distributors, to the consumer. But another general and inevitable law comes into operation just here. Superiority in quality necessarily involves a proportionately higher cost of production. As an illustration, Digitalis, throughout its collection, preparation, preservation and transportation is an article of merchandise simply, and continues to be so through four or five different merchants, until it reaches the hands of the special and ultimate variety of merchants, the pharmacist and the physician. These latter change the whole character and interest of the commodity. It is no longer simply merchandise in the common acceptation of the word merchandise, but has acquired another kind of value and importance from the fact that the pharmacist and physician are the direct and close representatives of numbers of patients suffering from diseased heart-action curable or controllable by this agent. Now Digitalis which is collected only in the proper season of maturity of the plant, and from second year plants only;—which is dried with proper skill and care;—packed and transported so as to avoid damage,—internal as well as external;—preserved so as best to avoid change, and not held for price until damaged by age, costs much more all along the whole line of its various markets than the same drug mowed down with less regard to season and age of plant, and pushed through the markets with least possible expense. Yet to the dealers, both are simply Digitalis,—the merchandise,—to be bought as cheaply and sold as dearly as practicable. Digitalis is rarely used in substance, so somebody along the line of its markets, while it is simply merchandise, and in order to make money by it, converts it into powder, or into fluid extract or extract. Up to this point there has been a fair, but not entirely trustworthy chance of discriminating between good Digitalis and bad, but here all, or almost all landmarks of quality and even identity are lost, so that the most expert pharmacist and physician cannot tell whether the preparation is made from good or bad Digitalis. If two preparations, one from good and the other from bad Digitalis, reach the physician or his patient at the same cost, those who supplied them,—all the way along the line of distribution,—will have made more money upon the bad than upon the good; and every discrimination of quality being impossible each dealer will favor that kind upon which he makes most money, and will discourage and disfavor the sales of that upon which he makes least money, in proportion to the smallness of his profits. This, as a general rule of trade, is inevitable, and the rule of itself is not immoral nor bad. In certain directions where the applications of medicines and of food are involved, a distant and not very distinct immorality and injustice are discoverable, but they are commonly too remote to have a strong influence in the intense struggle and competition of trade.

The pecuniary interests of merchandising, although by no means the only important interests recognized, are yet perhaps the safest and the surest upon which to rely for persistent uniform results, and if this be true the best way to secure superior quality in merchandise is to secure, or insure for such a quality superior profits to the dealers. Make it the pecuniary interest,—not only of one dealer or manufacturer, but of the whole line of dealers and distributors from producer to consumer,—to offer superior quality and then it will be done, and the stock of good supplies will not lie idle in the few principal markets, from difficult accessibility, but will be freely distributed wherever there is a demand for them, and by free distribution and easy access the demand will constantly increase, and the natural tendency will be to keep up the quality for the sake of the profit, and the multiplication of profit by increased demand.

To resume the illustration by a single article of the materia medica, suppose the skilled collector of Digitalis could command 20 cents per pound for his product against 10 cents for the common inferior drug, this would support and encourage progress in his superior skill and care. Then suppose the second owner or dealer should buy both kinds at these prices, and in selling to third hands, make 25 p. c. profit on each This would be 5 cents per pound on the good and 2½ cents on the inferior, and he need handle only half as much of the good to make the same amount of money as on the inferior, or in handling the same number of pounds of each would make nearly twice as much money on the good. Then, for the sake of brevity, suppose that two or more middlemen or distributors be avoided, and the pharmacist has the choice between Digitalis at 25 cents and at 12½ cents per pound. If he should buy some of each kind, and make powder, fluid extract and extract separately from both kinds, the one set of preparations would cost him much more than the other, and yet in sensible properties and to all easy tests they would be indistinguishable, the one set from the other. The question is thus narrowed down to how to induce the average pharmacist to buy the better quality rather than the inferior. The pharmacist's necessary expenses in proportion to the amount of his business are enormously heavy,—far beyond those of any other ordinary business, and he is usually cramped by over-competition and want of capital; still if he could make the same profit on both he would prefer the better and dearer drug. If in the average pharmacist the mercantile element should predominate over the pharmaceutical, he might use the inferior kind as being "just as good," or he might use both and offer the products of each at corresponding prices, keeping the profits equal. But if it be desirable to secure his strong and active preference for the better quality, so that he shall use that kind only and always, the best single inducement to offer him is better prices, and therefore more profit.

And here the physician is reached in his relations to his medical supplies. There is no doubt as to where the true interests of his patients lie, and their interests and his are the same. Therefore he may be considered as being virtually the consumer. Now let him inquire of himself how far he keeps the screw of price and cost of his supplies applied to the druggist and the jobber and the pharmacist, and he will then see that at least an important share of the responsibility for inferior medical supplies rests upon him.

He frequently, if not generally, knows what the prices are in first or second hands, from the price lists published in his journals, or sent to him from their sources, and he generally objects to an advance on these prices that is at all adequate to securing the best quality in his supplies. When the intermediate profits along the line of middle men or distributors are kept out of sight, as they are in the ready made prescriptions and specialties in general, alluded to in connection with the class of physicians to whom they are addressed, the difficulty about supply and profits is comparatively trifling. Let the class of physicians now under consideration accord or allow to the simple officinals of the materia medica the same scale of profits,—namely, first 10 p.c., then 15 p c. more, and then 10 p.c. more,—to those who handle these important agents along the line of their supplies, and they will probably soon cease to have much difficulty in obtaining such supplies as they need for their important art. The evils of ignorance and over-competition and even of mild degrees of fraud are so general as to seem at present inevitable, and the surest safeguard against their influences upon so important an interest as that of the sick and the suffering would seem to be to make the better way pay better. Physicians themselves are very poorly paid for their art and skill, yet their art and skill to their communities will come to be worth still less than they receive for them, if they gradually more and more lose control of the quality of the supplies, which render their knowledge and skill available in the treatment of disease.

HYDROCHLORATE OF COCAINE.

The last of a series of notes on this subject in these pamphlets was published at page 827 more than a year ago. Since that time much experience and information have accumulated, which it is the object of this note to record.

The supply of coca leaves in this market has steadily increased, and has always been greater than the demand, while the quality has also improved. Samples are still occasionally met with which, though fair in appearance, yield, on assay, very little cocoaine,—one or two have yielded none at all,—but the general average yield is increased. It is no longer rare to find lots which give .5 to .6 p.c. on assay, whilst others yielding .7 and even .8 p.c. are met with now as often, perhaps, as .5 and .6 p.c. were a year ago. This is doubtless due to improvement and care in the collection and drying of the leaves, and still more to the care in transportation since the discovery of how low a degree of heating and fermentation will diminish the proportion of cocaine, or destroy it altogether. It seems highly probable that very little coca is baled and shipped from either Bolivia or Peru, containing less than .6 or .7 p.c. of alkaloid, and that any which, on reaching the markets, yields less than this, has lost it on the way through heating and fermentation.

As it is rare here now that any considerable lots are bought without having been previously assayed, it is to be hoped that the easier sales and better prices realized on the better preserved leaves will have the effect of compelling still greater care in the drying and transporting the leaves. One or two shipments have been heard of which on assay yielded 1 p.c. of alkaloid, without any other marked difference from poorer leaves than that they had been dryer when packed and more carefully transported. From this it may be reasonable to infer that, in the near future, an increasing proportion of these high-test leaves may be expected, since it is pretty certainly within the easy reach of the producer and shipper to get them to market without any loss of alkaloid by the way, and as long as they are generally bought by assay the richer leaves will command the higher prices.

The prices also have changed very much, falling steadily as the qualities increased, so that quite recently sales of large lots of fair quality have been made at 16 to 20c. per pound, with a rumor of still lower figures, but the higher tests have always commanded much better prices, even up to 45c. per pound. As the trees yield three or four crops a year, and, under ordinary circumstances, continue this for twenty years or more, and as the labor and cost of gathering is not great, it seems probable now that these prices yield a fair return for the production, and that hitherto the middlemen have realized the largest profits. If this be so, their earlier profits must have been very large, as judged of from present prices.

This market history of decline in price in regard to the drug has, however, been greatly outdone in regard to the alkaloid and its salt. In the note written more than a year ago, page 827, it was estimated that 10 cents per grain was about as low as the writer then expected to be able to sell the hydrochlorate, as long as the heavy tax on alcohol and ether made these solvents so dear. Now the salt is sold at 1½c. per grain or less, and the percentage of profit is as large as it then was at 10 cents per grain. This enormous reduction is due to improvements and experience in the process of manufacture. Alcohol is entirely dispensed with in the process, and the quantity of ether used is so reduced as to be no longer a very expensive item. Of course, this writer does not know what other manufacturers are doing, but in his hands the process is now so simple, so easy and, so comparatively inexpensive that it seems incapable of much farther simplification, and the very great wonder is, that it has taken him so long, at such an amount of labor and expense, to reach the present result. Looking back over the past two years of work on this subject, it seems hardly credible that any ordinary degree of capacity and intelligence should have advanced so slowly, and yet this writer has the advantage of his very able assistant, Mr. John A. Dunn, to whom he owes much of the labor and skill of the present process. There are many alkaloids which are very easily decomposed or split up into other bodies whose relations to solvents are similar to the original alkaloids. This tendency to split up is by reason of the looseness of their compound molecules, or, so to speak, by the easily disturbed cohesion in their cleavage planes,—and cocaine is one of the most delicate and sensitive of these alkaloids in its tendency to change of character or to split. The splitting, in this case at least, seems to occur from the action of alkalies, and to be prevented by acids; and hence the use of acidulated alcohol in the former process of extraction, as given at page 719, and hence the tartaric acid in the process of Duquesnel and Wright in the extraction of aconitine. But many years ago Couerbe, and possibly others before him, and certainly others since, recommended the use of acidulated water for the extraction of some alkaloids, and this answers very well for cocaine.

The leaves are coarsely ground, moistened well with water, containing 5 p.c. of its weight of sulphuric acid, and packed in large stoneware percolators. They are then subjected to the process of repercolation, until the extract is very dense and very concentrated. This solution is well agitated with kerosene oil and an excess of carbonate of sodium. The liberated alkaloid is dissolved and held by the kerosene comparatively free from coloring matter and all other substances. It is then washed out of the kerosene by means of acidulated water, and again precipitated by carbonate of sodium in the presence of ether by agitation, when the alkaloid is practically colorless. From the ether it is washed out in fractions, —the first of which contains most of the remaining coloring matter,—by dilute hydrochloric acid. The nearly colorless fractions of this solution are evaporated while crystallizing in very shallow pans at a very low temperature with constant stirring, as described at page 724. The product is a granular, coarse powder of broken crystals, which when the larger lumps are crushed so as to pass through a No. 40 sieve, makes the nearly white, and very nearly pure anhydrous salt as sold by this manufacturer.

If the salt in this condition be dissolved to near saturation in warm and strong alcohol, and be set to crystallize, it will, within a week or ten days, yield a crop of distinct and compact crystals large enough to be seen distinctly by the naked eye. These, when washed free from mother liquor, with a little alcohol or ether, and dried, yield a nearly chemically pure anhydrous salt, and, were it not for what is to follow, this would be the only condition in which it should be offered for sale. But this salt, when offered for sale, should always be labeled as "Recrystallized." The waste and loss in making this salt are at present so great, and the advantages it has over the salt before being recrystallized are so very small, that the writer has never made it on a scale of more than a few ounces for trial. The advantages of it are chiefly in appearance. Tried side by side with the salt before recrystallization no therapeutic difference can be detected, nor can any be detected by the physiological test to be mentioned later. The chief disadvantage of the recrystallization is the loss in the process. By the greatest care yet attainable from 25 to 30 per cent. of the salt remains in the alcohol in an uncrystallizable condition,—that is, uncrystallizable from the alcohol. If the alcohol be slowly evaporated, a mixture of sticky dense amorphous salt and very small crystals is obtained, and this, if exposed to the atmosphere for a week or two, spontaneously crystallizes throughout, but the crystals are minute and powdery and very unlike the first crop. Therapeutically and physiologically, however, it is not discoverably different from the first crystals. Chemically, and in its reactions with chemical tests, it is very different; but the main difference here, in the process, is the difficulty of crystallization; and this separates the pure salt into two distinct parts or conditions, and these, for the purposes of this paper will be designated as the easily crystallizable and the difficultly crystallizable condition of the salt. It has only been through recent investigations and improvements in the process of manufacture that the comparatively large and compact crystals have been obtained, and it is not many months since their first appearance in the market so as to be used on the large scale, and as yet but one manufacturer here offers them. All the best work of the salt as an anæsthetic was done before they were accessible, and since they have been accessible they have not shown any therapeutic advantages. The reasons why the writer does not offer them for sale are, first, that they have no therapeutic advantages, and next, because the difficultly crystallizable part of the salt would either have to be wasted, and thus very much increase the cost of the easily crystallizable portion, or have to be sold in the granular crystals, as is done by other manufacturers of the larger crystals, thus making the complication of two kinds of salt from one maker, without discoverable difference in thereapeutic value between them.

It would seem that with so much chemical difference there should be a therapeutic difference, and yet there are stronger illustrations than this among the sensitive alkaloids and their salts, of chemical differences without therapeutic. For instance, the dark liquid, amorphous hyoscyamine is therapeutically as effective as the nearly colorless crystals,—many careful observers, who have used much of both kinds, say more effective.

There is another way of separating the easily from the difficultly crystallizable portion of the salt. It happens that the easily crystallizable condition is soluble in chloroform in the proportion of about 1 part in 33 by weight, or 1 gram. in about 22 c.c. of chloroform of s.g. not less than 1.47—while the difficultly crystallizable condition is much more soluble,—perhaps almost indefinitely soluble. Now, if the salt as sold by all manufacturers here, made by stirring down to dryness during crystallization, be washed with chloroform which has been saturated with the easily crystallizable condition of salt, the more soluble condition can be washed out, and separated more perfectly than in any other way yet found. And upon this behavior is based the chloroform test to be described farther on. But this is also a somewhat expensive process, though much less tedious and troublesome than the separation by alcohol, and it yields the same results, so that, under the circumstances, it seems at present much the best practice not to separate the salt into its two conditions, but to sell them together, and this policy is strengthened by the observation that in the processes for the separation, the proportion of easily crystallizable salt is diminished and the other increased, while there is at the same time a sensible decomposition of alkaloid indicated by increased acidity.

This writer began the manufacture of cocaine salt in October, 1884, and up to October, 1886, used 177 bales or 22,285 lbs. of coca leaves. The highest price paid was $1.50 per lb. and the lowest 30c., the average being 50.5c., and the total cost $11,269.62.

The first salt sold in October, 1884, was only a few grains, and a few ounces of 4 p.c. solution, but from that time the sales have increased steadily, with occasional fallings off, as other manufacturers would attract the buyers by reduced prices, before the reductions were discovered and met. The tendency of the price has been steadily but rapidly downward, and where the "bottom" price to confidential, close buyers of large quantities in bulk, now is, it is impossible to tell, but $5.00 per ounce has been heard of for nameless brands, and the secondary or difficultly crystallizable product of the makers of the larger crystals. In this, as in all medicines, no matter how important, there are a great many buyers who make price the first consideration, and such buyers who know the whole market well, are probably now buying and selling hydrochlorate of cocaine of fair appearance, and not very bad quality, at $5.00 per ounce, or, may be, even less. But, under present circumstances, a good quality cannot be made, and pay even a moderate manufacturer's profit, at that price. Yet, very much of what is sold at the lowest prices of any, comes from abroad and pays a heavy import duty.

The total quantity, calculated as hydrochlorate of cocaine, yielded by the above-mentioned 22,285 lbs. of coca, was 535,252 grains, or 76 lbs. 7½ ozs. nearly, and the average yield was 24.02 grains to the avoirdupois pound of leaves.

Many hundred pounds of good coca were lost and wasted, first in finding out how to make cocaine at all, and afterwards in learning how to do it well, and in reaching the present process; and it is almost certain that, with the present process to start with, the yield would have been more than double, as there was, doubtless, more than double the amount of alkaloid in the coca.

In the early part of its career, there was a great deal of hydrochlorate of cocaine sold at $1.25 per grain, but the writer never sold any of his own make at over 75c. per grain, and this price has been gradually reduced in the two years to less than 1½c. per grain. As soon as the processes of manufacture became fairly productive, the competition between manufacturers to make sales by reductions in price became very sharp. The writer never entered into this competition in price, but by reducing his price, as improvements in his process would warrant, has never been far behind the lowest prices of the market. The sale of the above-mentioned product of nearly 76½ lbs. yielded about $26,906.00, or about 5.03c. per grain average, and as the cost of the leaves was about $11,270.00, the apparent profit was $15,636.00, or nearly 139 p.c. This, however, is not profit, but merely the difference between the cost of the coca as one of the materials used, and the proceeds of the sale of the product. During the whole of the first of the two years, alcohol was used as the menstruum for the extraction, and this single item of material, cost far more than the coca. Indeed, throughout the first year, the process gave a continuous loss of money and work, although this was the period of highest prices. At the end of the first year the price was 10c. per grain, but there was little or no profit in the manufacture until the better process was reached; and, as above stated, the profit is better at 1½c. per grain than it has been at any higher price, and if coca leaves do not advance from the present low prices, there may be room for a still further decline in price, whilst a fair profit is maintained, provided the quantity sold should not fall off, since it is the quantity in which such articles are made that controls the cost of production. The quality has also improved with experience and skill in working the process on a large scale, so that now the salt made by this writer is therapeutically unobjectionable, while in appearance it is very nearly colorless, and very nearly free from decomposition products. It may not be therapeutically any better than it was a year ago, but it is many shades whiter, and contains less of the split alkaloid. Indeed, for all practical purposes it is supposed to be as good as it can be made.

The process for assaying the leaves has been improved quite as much as the process of manufacture. As a rule, all assay processes should be as nearly like the processes of manufacture as practicable. With organic substances they rarely, if ever, attain to the accuracy of inorganic substances, because the products of assay are so complex in composition and so easily decomposed ; and the approach to accuracy in result will generally depend upon the process, and the skill with which this is applied. A manufacturer will generally assay his crude material by his own process of manufacture, because then he will get out of his material about what he is led to expect by his assay. But another manufacturer may get out more or less as his process may be better or worse, or be applied with more or less skill. But generally the same process, used with the same skill, will give slightly better results on the manufacturing scale than by the assay. This general result of assaying is, however, not realized with coca, probably because in such sensitive alkaloids some part is decomposed and lost.

The writer's present process of assay is as follows :

The coca leaves are ground into coarse powder, 20 or 30 meshes to the inch. Of this powder 100 grammes is moistened with 100 c.c. of water, containing 5 p.c. of sulphuric acid, and is packed moderately in a cylindrical percolator, and percolated to 500 c.c. with the same acid water menstruum. This percolation is best done by means of a Sprengel water pump into a flask marked at about 500 c.c., and this amount of percolate will generally exhaust the coca sufficiently even when the leaves are of the thick Bolivian variety. A portion of the stock of the acid water used is then balanced against a portion of the stock of re-crystallized carbonate of sodium, and it will generally be found that 6 to 6.5 grammes of the crystals are required to saturate 100 c.c. of the acid water. The percolate is then measured off into a large beaker or other similar vessel, and 50 c.c. of kerosene added to it, and the whole well stirred together. Then as much of the crystallized carbonate of sodium is added as would saturate the percolate if it was all acid water, the sodium salt being added little by little with constant vigorous stirring. In order to precipitate the alkaloid completely, the sodium salt is required in considerable excess, and the difference in acidity between the percolate with its large percentage of extract and the acid water, gives about the proper excess. The kerosene is very thoroughly and repeatedly stirred into the mixture during four or five hours of digestion, and is then separated by means of a separatory funnel or a small syphon. Then 25 c.c. of fresh kerosene is added to the percolate and the stirring, digestion and separation are repeated twice, making three washings with the kerosene. If an emulsion should form between the percolate and the kerosene it will lie next above the percolate in drawing this off, and should be drawn off into a separate vessel with the final washing. A little dry filter paper pulp, or a little asbestos, or sand stirred into this emulsion will break it up so that the kerosene can be separated completely, when it is added to the larger portion. If the percolate and the kerosene be shaken together, instead of being stirred as above directed, all or nearly all of the kerosene will be made into an emulsion. On standing two or three days this emulsion will separate wholly or partially, but as the operator can never tell before hand whether it will separate completely or only in part, it is better not to wait, but rather to separate it as directed. Then by stirring rather than shaking, the amount of emulsion is reduced to a minimum, and if the stirring be well done, the percolate is washed free from alkaloid, and this latter is practically all held dissolved in the kerosene. But if the operator wants to be assured that he has washed out all the alkaloid from the percolate, let him add to the latter about two grammes more of carbonate of sodium and 25 c.c. of ether and again stir, or shake and separate. The residue left on the evaporation of this ether should give no cocaine impression on the tongue, nor any saturating power to a very minute quantity of very dilute acid. The 100 c.c. of kerosene holding the alkaloid in solution, is then shaken vigorously in a separator (see page 786) three times,—twice with 10 c.c. of the acid water, and the third time with 5 c.c. of water. This washes out practically all the alkaloid as sulphate, and leaves the kerosene ready for another assay. To the

25 c.c. of solution of sulphate of cocaine contained in another separator 10 c.c. of strong ether is added, well shaken, and then a moderate excess of crystals of carbonate of sodium. After the effervescence, this is well shaken and the ether separated. The solution is again washed twice with 10 c.c. more of ether each time. All the ether is then collected, entirely free from even a fraction of a drop of the solution, in a beaker of at least three times the capacity of the ether. From this the ether is evaporated and the alkaloid is left in the condition of a light amber-colored varnish on the bottom and sides. If a capsule be used instead of a beaker, or if too small a beaker be used, the ethereal solution is liable to creep over the edges and be lost. As soon as the beaker is free from the odor of ether, it may be weighed, and the tare subtracted will give the weight of cocaine obtained from the 100 grammes of coca. This weight varies, in the writer's experience, between a few millegrammes, which is called 0. and .892 gram., equal to .892 p.c., the highest result yet obtained. If the beaker, with its varnish-like coating, be set aside, there will appear, in a longer or shorter time—generally within five or six hours—minute centres of crystallization, and these will slowly extend until within 24 or 48 hours the whole varnish-like coating will be converted into a white crystalline crust. This crystallization takes place without any discoverable change in weight when the beaker is kept on a balance sensitive to one-tenth of a millegramme.

During October, 1886, seventeen different lots of coca, aggregating about 410 bales, or more than 80,000 lbs., were assayed by this process, with results varying between .420 and .826 p.c., and the prices asked for the lots varied between 16 and 45c. per lb. being generally in proportion to the cocaine value. Of these, four lots, aggregating about 14,000 lbs., were bought, assaying .594—.612—.626 and .793 p.c. at 16, 18 and 20c. per lb. Of these that of .793 p.c. at 20c. was cheaper than the .594 p.c. at 16c. The latter, if at 15c., would have been at the same cocaine value as the .793 p.c. at 20c., but would still have been dearer, because each required the same amount of material, apparatus, time and labor in extraction, for three-fourths the product in the poorer coca.

In the following examination of the cocaine of the New York market, the hydrochlorate only was used, as this salt fulfills all the purposes to which the cocaine can be usefully applied, and fulfills them better than any other salt.

The writer knows of only four actual manufacturers of cocaine in this country, although there are others who claim to manufacture. The markets of this country are mainly supplied from Messrs. W. H. Schieffelin & Co., McKesson & Robbins, The N. Y. Quinine and Chemical Co. and the writer. Another source of supply for a small proportion, is the well-known Darmstadt house of E. Merck, and occasional parcels are met with from Messrs. Howards & Sons, of London. Another foreign make,—name unknown,—is imported and sold in considerable quantities. From the fact that its source is unknown to the writer, and that it pays the high rate of import duty, and still competes in price with the salts made here at a profit much below the duty, it was not taken into investigation. Two of the above-named makers each sell two different kinds of salt, so that the four makers produce six brands or kinds. Then a brand largely sold is that of Messrs. Parke, Davis & Co. These seven, with those of Merck and Howards, make up the nine brands that were examined in this investigation. Before the examination had proceeded far, it was found that one of the brands of the N. Y. Quinine and Chemical Co. was so nearly identical with that of Parke, Davis & Co., that different parcels under the same label differed quite as much as parcels bearing the different labels; and precisely the same conditions were found between one of the two brands of McKesson & Robbins and that of Merck, and throughout the whole investigation these four brands were found to represent only two kinds. Original vials of all the nine brands were bought four times or oftener at intervals of a month or less during the five months of this investigation, with the exception of Howards, and of this only one vial was examined.

These nine brands, by their sensible properties, fall naturally into four groups. Two kinds of granular crystals, and two kinds of larger crystals. In the first group there are four individuals; in the second, two; in the third, two, and in the fourth, one. The first group contains the granular brands of each of two makers of the second and third groups. In the market the four groups are not unfrequently classed as two, and for business purposes, and in circulars and advertisements, they are commonly alluded to as crystallized and amorphous. When the makers of the larger crystals first put them on the market, it was common to hear all the others condemned as being amorphous, and therefore, inferior in quality, but since they have each put a granular variety into the market, less has been heard in discriminating praise of the larger crystals. As a matter of fact, all are really crystalline, and it it is extremely doubtful if an amorphous salt can exist for any considerable length of time.

Both the alkaloid and the salt are often seen in an amorphous condition, but this condition is temporary only, and either in crystallizing, or where subsequently submitted to the action of solvents or precipitants, it appears to separate into two conditions, the one capable of crystallizing in large crystals and the other only in small granular crystals, both crystallizing very slowly and with difficulty, but the latter condition with most difficulty.

The original vials bought in the market at the before-mentioned intervals of time, varied very much from each other of the same brand, the appearance and true quality of each brand showing much progress. Indeed, the two vials of every brand, bought five months apart, would hardly be recognized as from the same maker, and the improvement has been about the same in all, as skill and experience accumulated in the manufacturing processes.

Almost all are described in circulars and advertisements as being colorless, but not one is really colorless, as shown by their solutions, though some are very nearly so.

Almost all are described as neutral, yet not one is actually neutral to good litmus paper, when in strong solution, and in this respect, as in color, they differ considerably.

All were fairly free from dust particles, though none sufficiently free for use in solution without filtration.

The groups may now be separately considered as Nos. 1, 2, 3 and 4, the best specimen of each group being taken as the type, and the best and latest parcel of each brand being used for description and testing, and all the testing done as nearly as practicable under the same conditions.

No, 1, as the type of the first group, is in a rather fine granular powder of a pale cream color, not very nearly white. Dissolves easily and quickly in an equal weight of water, giving a transparent solution of the color of brandy—the darkest of any of the solutions by many shades. This 50 p.c. solution was slightly acid to test paper on first contact, and did not become more acid on prolonged exposure to the air. Of all the brands, only one was more acid, and this one of the same group.

Under the microscope, with a four-tenths objective, by transmitted light, it appears as a granular powder of angular fragments of small crystals, with transparent points and edges, very few of the fragments being small enough to be translucent. When wetted on the slide with a minute fraction of a drop of alcohol, rapid currents are established around the particles, and as these are rapidly disintegrated and dissolved they are very distinctly seen to be fragments of transparent crystals which are rounded by the currents of liquid, as they very rapidly disappear by solution. When all the masses in the field are disintegrated and dissolved, the transparent solution is invisible and remains so for some time, the alcohol having left the salt in the amorphous, sticky, varnish-like state. Then granular-looking islands are seen, which obstruct the light, and around their edges two or more forms of crystals appear. At first, this was supposed to indicate that two or more substances or salts were present, crystallizing in different forms. But a few experiments with more or less water present with the alcohol, proved that the different forms of crystals were due to different degrees of hydration. That is, as the alcohol evaporated more rapidly than the water, that which remained became more and more dilute, thus yielding different forms of crystals. The crystal which seems to form from thin films of alcohol, while that solvent is still strong, is a hexagonal plate with two of its parallel sides longer than the other four. The later crystals which form in the varnish-like film after the alcohol is evaporated are needles with bevelled ends, in stellate groups. This is supposed to be the hydrated form of crystal, because in a few hours both the alcoholic plates and these have all disappeared, and have been replaced by a confused mass of crystals in which no signs of either plates or needles are to be found,—and this form is permanent. It is, therefore, supposed to be the anhydrous crystal, and to represent group No. 2, while the needles represent group No. 3. The hexagonal plates that form from this No. 1 group are very small and without sharp angles,—many of them barrel-shaped and others nearly circular.

A minute drop of the 50 p.c. solution, evaporated on a slide over sulphuric acid, gave a varnish-like film fissured irregularly in all directions, just as a solution of a resin would dry, and crack in drying. This film exposed to the air for a few hours begins to crystallize from centres, and in two or three days becomes entirely crystallized.

Exposed to the air on a watch-glass for 48 hours, different parcels all gained in weight from .175 to .200 p.c. Warmed in the air for 48 hours at 37.7° C.=100° F., there was still a small gain of about .100 p.c. Exposed for 12 hours at temperatures between 71 and 82° C.=160 to 180° F., it lost 1.5 p.c., and then exposed again at ordinary temperatures for 12 hours it regained 1.275 p.c. of this loss.

Heated in a thin test tube in a glycerin bath, at 145° C.=293° F., it became brown, and had lost 6.196 p.c. without melting. When the bath arose above that temperature, melting and frothing began, and at 152° C.=306° F. the whole was melted, with a strong odor of benzoin and a total loss of 7.521 p.c., and the fused mass, when cold, was transparent and resin-like, and of a dark amber color.

When ·4 gram. was shaken in a large tared test tube with successive additions of chloroform it was not all dissolved until about 4.40 c.c. of chloroform was used. When to this solution three times its volume of stronger ether was added, and the whole well shaken for several minutes or until the liquid was quite transparent, the salt collected upon the walls of the tube in the form of a whitish gummy coating. After standing half an hour, the transparent liquid was poured off into a tared beaker, and both tube and beaker were dried at 100° C.=212° F., and the dry precipitates were then weighed. The gummy coating had become entirely crystallized and weighed .3844 gram., and the residue in the beaker weighed .0108, equal to 2.70 p.c.

When 1 c.c. of concentrated sulphuric acid was poured upon .2 gram. of the salt in a test tube, brisk effervescence occurred, with a strong odor that resembled chlorine and hypochlorous acid. A slight amber color was at once developed, and as the solution of the salt progressed this color changed and deepened to a deep brownish red, or deep claret color, the liquid being quite transparent. On standing half an hour the red became slightly browner.

The permanganate test of Dr. F. Giesel was in all cases applied critically in the following manner:

When .05 gram. was dissolved in 1 c.c. of distilled water, and 1.1 c.c. of decinormal solution of potassium permanganate added, precipitation occurred at once, and for a few seconds was of a red color, but within 15 seconds it was all of a brown color without any admixture of red,—not even a reddish brown. In 5 minutes 8 c.c. of distilled water was added to this and the whole well shaken. The brown flocculent oxide of manganese then gradually settled out, leaving a transparent solution of a brownish tint almost colorless, within an hour. It, therefore, did not stand this test at all, in any degree.

The physiological testing was made as follows: For the comparisons a 1 p.c. solution was made from a salt of standard purity.

One minim of this solution in one fluidrachm of water, held in the anterior part of the mouth for one minute, the mouth having been just previously rinsed out, gave a distinct sensation, short of numbness, but suggestive of it, to three persons out of four,—the fourth getting only a slight bitter taste.

As one minim of such solution weighs nearly a grain, or about .063 gram., this test would contain .01 grain, or .00063 gram., in 5,600 times its weight of water.

One minim of the 1 p.c. solution in 30 minims of water, held in the mouth in the same way for the same length of time, gave a distinct sensation to all.

Equal measures of 1 p.c. solution and water give a .5 p.c. solution, or one that contains 1 part of salt in 200, and one minim of such solution, will contain .02 grain of the salt. One minim of this solution delivered carefully and slowly from a fine-pointed pipette, upon a strip of filtering paper .75 inch wide, can be made to wet the strip equally for about 2 to 2.25 inches of its length. This wetted portion when dried will contain .02 grain of the salt equally distributed through the paper. Then if the paper be ruled off and cut into 10 squares of equal size, each square will contain one two-thousandth of a grain (.0005 grain) of the salt. One of these small squares laid upon the anterior part of the clean, moist tongue, and the tongue then held against the roof of the mouth for one minute and then the paper discharged, a very distinct impression is obtained, and this, after a few trials, will teach the observer what to look for, in a lesser degree, in using more dilute solutions.

Successive dilutions of 1 measure of 1 p.c. solution in 1.5,-2,-2.5 and 3 measures of water, treated in the same way, gave small squares containing $\frac{1}{2500}$, $\frac{1}{3000}$, $\frac{1}{3500}$ and $\frac{1}{4000}$ of a grain.

Eight persons out of ten got a distinct impression from all the squares excepting the last two, and four out of the eight got an impression from all.

From the last dilution, $\frac{1}{4000}$ grain, one person got the impression every time in over twenty trials, and another got it every time in four successive trials. After becoming used to the faint impression to be watched for, seven of the ten persons could be repeatedly tried with blank squares of paper, with but few failures in distinguishing them from those which contained the salt. Yet two of the ten failed in this cross-testing up to $\frac{1}{2000}$ grain.

It was next found that a difference of 10 p.c. in the amount of salt present in these dilutions could not be detected with absolute certainty by the more sensitive of the observers, and only three detected this difference, yet still without positive certainty. Hence, differences of 10 p.c. or less in quality are not discoverable in this way, and it may, therefore, be reasonably inferred that such differences could not be discovered in the therapeutic use of different salts.*

Thus it will be seen that this physiological test, though useful, is by no means a closely discriminating test.

When applied to this specimen No. 1 now under consideration, the specimen withstood the test only fairly well. That is, some difference between the impression from the standard was indistinctly noticeable, and yet was noticeable.

All the above mentioned testings of No. 1 were applied to the best and most recent of the parcels bought of this make. Each parcel bought was better than the one a month or more before it, and this the best of the series of four.

Three other of the nine market specimens embraced in this investigation,—namely, that labelled as "Powdered," and that of Howards & Sons, and a third in granular condition,—were as nearly like it as were the different parcels of each brand like each other. Of the London makers, however, there was but one specimen. In granular condition, color and solubility, it was very similar to No. 1. But in color the solution was not so deep, and it was more faintly acid. Under the microscope the appearance and reactions were similar to No. 1. On exposure to the air, and on being warmed and heated it was also very much like No. 1. In solubility in chloroform, however, it differed materially from No. 1, requiring 6.50 c.c. of chloroform against 4.40 for No. 1, and the salt recovered by precipitation from chloroform by ether weighed .3976 gram. from .4 gram. of the salt, and the residue .0100 gram. or 2.5 p.c.

The sulphuric acid testing gave a deep red, about the same depth of color as No. 1, but with less of the brown tint.

With the Giesel test by potassium permanganate it stood very much better than No. 1, the solution retaining much of the red tint in the prevailing brown for more than an hour. Indeed, the reaction with this test was nearly as good as with any specimen of the nine, and much better than with six of them.

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* Fluid extract of coca was tested in the same way, and it was found that a well-made fluid extract from coca which yielded .5 p.c. of cocaine by assay, made without heat, would give account of a rather larger proportion than by assay. From this it is concluded that the fluid extract should not contain less than .5 p.c. of alkaloid, and should be a full equivalent of a solution of the hydrochlorate of cocaine of the strength of .5 p.c.

By the physiological test it was indistinguishable from No. 1.

The best and latest specimen of the "Powdered" salt was very different from previous specimens under the same label. It was very similar to No. 1 in appearance and solubility, but the solution was more acid, and most acid of any specimen examined, the blue litmus paper being quite sharply though not brightly reddened on first contact with the 50 p.c. solution.

Under the microscope it was not distinguishable from No. 1.

By the exposure to air it lost .325 p.c., whilst No. 1 gained. But upon heating, the behavior was very similar to No. 1.

The solubility in chloroform of different parcels under this label was very different. Of the earlier parcels .4 gram. dissolved at once to a clear solution with 2 c.c. of chloroform, and in a few hours this solution became a dry solid. The latest specimen required 6.20 c.c. for solution, and the solution only partly solidified on the walls of the tube above the liquid,—that is, where a part of the chloroform had evaporated off.

The sulphuric acid test gave an amber color not so deep as the brown of No. 1.

With the permanganate test the rose-red color was retained in fair degree for ten minutes, and then the change to brown became more rapid, and all red tint had disappeared from the brown color at the end of half an hour.

The physiological testing was practically identical with No. 1, or, if any difference, it was favorable to No. 1.

The remaining specimen belonging to this No. 1 group, and sold by the other maker of the larger crystals as "Powder" or amorphous salt, though entirely crystalline, was inferior to the last described excepting in color, this being quite white or free from color. The .4 gram. was dissolved by 5 c.c. of chloroform, the precipitated salt weighing .3850 gram., and the residue .0116 gram., or 2.90 p.c. In other respects it was very much like the kind last described.

Specimen No. 2. The latest and best parcel of this make was in colorless, hard, shining, distinct crystals of such size as to be all visible to the naked eye, very easily but somewhat slowly soluble in an equal weight of water, owing to the hardness of the crystals. The 50 p.c. solution when in small quantity was almost colorless and was very bright. This solution was very faintly acid to blue litmus paper on first contact, becoming very slightly more red after a few minutes' free exposure to the air, ranking fourth in the degree of acidity.

Under the microscope no distinct crystalline form can be seen, most of the distinct transparent pieces appearing as confused fragments of plates, with edges generally slightly rounded as from having been washed by a solvent liquid. When a fraction of a drop of alcohol was added on the slide, the smaller fragments were thrown into active motion as they pretty rapidly dissolved, and then as the alcohol evaporated at the edges of the spot, the hexagonal and barrel-shaped plates appeared and often filled the field. These plates were of much larger size than those of No. 1, and much more quickly formed, and they soon coalesced into confused masses wherein no lines of the original form were discoverable. Then as the alcohol passed off leaving only water, the crystallization changed entirely first into groups and masses of stellate needles, with obliquely bevelled ends, and finally into confused masses somewhat like the original crystals.

Exposed to the air for 48 hours different parcels all lost weight, the last and best parcel losing 2.85 p.c. Heated in a glycerin bath to 145° C., it suffered an additional loss of 1.72 p.c. without melting. Began to melt at 155° C., and was all melted with little frothing at 160° C., with a strong odor of benzoin, and with a total loss of 9.45 p.c. The fused residue was of a full amber color and quite transparent. When .4 gram. of the finely powdered crystals was shaken in a test tube with successive additions of chloroform, it was not all dissolved until 8 c.c of chloroform was used, and the tube allowed to stand overnight.

When to this solution three times its volume of stronger ether was added and the tube well shaken for five minutes, or until the liquid was quite clear, the precipitated salt in the case of some parcels collected entirely upon the sides of the tubes in a sticky condition. In other cases a part collected on the tube, while another part remained loose and granular, and fell to the bottom when the tube was at rest. This precipitated salt appeared to become crystalline within an hour or two, even before the liquid was poured off from it. The liquid drained off into a tared beaker and evaporated left a residue, which was not visible to the eye, and weighed .0056 gram., or 1.40 p.c. The salt when thoroughly dried in the tube weighed, in different trials, .4008 to .4000 gram., and always as much as the weight originally taken, and was always crystallized throughout.

When 1 c.c. of concentrated sulphuric acid was delivered upon .2 gram. of the salt in a test tube, brisk effervescence with a strong chlorine odor was observed. When the effervescence had ceased and the tube stood for half an hour, the liquid varied in different parcels from a pale reddish straw color to a pale wine color. On longer standing the color became somewhat deeper.

With the permanganate test, applied exactly as in No. 1, excepting that a similar test tube with the same permanganate solution without any of the salt, was kept in the stand beside it for comparison of color,—the color changed slightly at once, and continued to change to a brownish tint, slowly, until it became brown and finally colorless. At the end of an hour it was red, but a brownish red; in 2 hours a reddish brown, and in 4 hours a yellowish brown, with no redness of the brown, and after 48 hours a brown precipitate had all settled out and the liquid was colorless. This brown precipitate commenced to form from the very first, so that the red solution was never clear, and the permanganate purple was only retained for a short time, but in some parcels longer than in others. Treated with .5 c.c. more of permanganate solution the same changes occurred, and this repeated twice still became colorless after an interval of a night.

The salt precipitated from the chloroform solution by ether retained the reddish color longer when subjected to this test. The repeated decomposition of permanganate by this purest of all the groups, chemically, is supposed to prove that the salt, even in its easily crystallizable state, is decomposed by the permanganate.

By the physiological test it was hardly distinguishable from No. 1, and not distinguishable from the standard. Repeated cross testings, on different days, developed a difference so slight, that at last it was not settled beyond doubt whether the impression was stronger than No. 1 or not.

One of the nine market specimens, namely, that of Merck, of Darmstadt, was so nearly like this No. 2 as to be, so far as these testings go, identical. The same appearance and form of crystal and the same reactions throughout; the four different parcels examined differing quite as much among themselves as from No. 2, and the last of the four, the best, as in Nos. 1 and 2, and the last vials bought agreed much more closely than any previous ones. The difference in price, however, was remarkable. No. 2 cost $7.50 per ounce avoirdupois, and this, $16.50. The import duty does not account for one-fourth of this difference.

No. 3. This is very unlike any of the other groups, and distinguishable at sight. It is in small acicular crystals more or less effloresced, differing in this respect, and in the size of the crystals in different parcels. The salt is colorless, and almost instantly soluble in an equal weight of water; this 50 p.c. solution being of a pale straw color, and distinctly though not strongly acid to litmus paper on first contact. Less acid than No. 1, but more acid than No. 2, ranking third in acidity.

Under the microscope the salt appears as broken-up bundles of needles more or less studded over with effloresced powder. Wetted with a fraction of a drop of alcohol on the slide, it is disintegrated and dissolved with rapid movement, showing fragments of two forms of crystals. The recrystallization, as the alcohol evaporated, passed through practically the same stages, and gave the same forms of crystals as Nos. 1 and 2, but the intermediate plates were intermediate in size between those of Nos. 1 and 2, and were more nearly rectangular.

Exposed to the air for 48 hours, all the parcels of this salt lost largely in weight, but no two parcels lost alike. The lowest loss observed was 6.72 p.c. and the highest was 8.62 p.c. But a beautiful exhibition sample of silky crystals, with no appearance of efflorescence, lost over 10 p.c.

In the glycerin bath the salt melted with frothing at 148° to 150°C., fusing to a dark amber-colored liquid, with a total loss of 12.65 p.c.

When .4 gram. was treated with successive additions of chloroform, and the tube allowed to stand for a few hours between the small additions toward the last, it was found to be soluble in 5.40 c.c. of chloroform. This solution, precipitated by the addition of 16.2 c.c. of stronger ether, the salt collected in an amorphous gummy condition upon the walls of the tube. The clear liquid was poured off into a tared beaker and evaporated to dryness, when the residue was found to weigh .0114 gram., or 2.85 p.c. The sticky layer on the inside of the tube crystallized at once, and when dry weighed .3848 gram., the sum of these weights being .3962 gram. from the .4 gram. as taken.

The test by sulphuric acid gave a very rapid solution of a full amber color with reddish tint, with the characteristic reaction and chlorine-like odor.

The permanganate test was applied as in No. 2. The color was not purple at any time, but dull rose-red from the first, changing considerably in the first few minutes, and then more slowly, becoming of a brownish red, and finally brown, with no red tint in about 35 minutes. Treated again with .5 c.c. permanganate solution, and this repeated, the same results were obtained, but at longer intervals. The portion of salt precipitated from the chloroform solution by ether, when tested in this same way, remained reddish much longer, being a very red brown at the end of an hour. Different parcels of this make reacted very differently with the test, the above description being from the latest parcel. A beautiful exhibition sample of this make, in silky crystals, when tested by this method, remained of a very red brown for an hour and a half.

The physiological testing gave no marked difference from the standard or from Nos. 1 and 2. But whatever difference there may have been was against this salt. It is seen from the above given reactions that this is a hydrated salt, in a more or less effloresced condition, while all the others are anhydrous, and that it easily parts with proportions of water, varying from 6 to 9 p.c. Everything else being equal it must, therefore, of necessity, be 6 to 9 p.c. weaker than the others, and that the physiological test does not show this deficiency detracts much from the value of this test.

Another of the eight brands of the market that is very largely sold,—namely, that of Messrs. Parke, Davis & Co. of Detroit, was found to be identical with this No. 3. That is the four parcels bought at different times varied quite as much among themselves as they did from the four parcels of No. 3, while the latest parcels of each, bought near the same time appeared absolutely identical. And these two are the only hydrated crystals ever met with in this or any other market.

No. 4. This salt was in the condition of a coarse granular powder. It was practically colorless, though not absolutely so, and dissolved easily and quickly in an equal weight of water. The 50 p.c. solution was transparent and bright, and of a very pale straw color. The solution was very slightly acid to litmus paper on first contact, just perceptibly changing the blue. This acidity was less than in any of the others, and changed less on exposure to air for a time, ranking lowest in acidity of the entire nine parcels.

Under the microscope this salt appeared as a granular mass of fragments of crystals so broken up that the form of crystal could not be recognized,—occasional transparent fragments in the field appearing as broken up plates, the edges and angles of fracture being fairly sharp. Moistened on the slide with a fraction of a drop of alcohol the masses were disintegrated with very active motion, and as they were washed away showed the distinct transparent fragments of crystals of various shapes and sizes, down to granular particles without recognizable form, under this magnifying power. As the alcohol evaporated crystals of various forms pretty rapidly appeared, but very soon the prominent forms were various modifications of the hexagonal plates and the stellar needles. The plates were more distinct in form than in No. 1, and less distinct than in No. 2, and often appeared so rounded at the angles and bulged at the sides as to appear round or oblong. These, however, soon coalesced and disappeared, and as the slide became dry the spot wetted became granular excepting at the edges, and here there was, where the solution was shallow and thin, a fringe of radiating needles; and in a few hours the whole spot assumed this crystalline condition. This salt was thus shown to be of the same general character as group No. 1, though more crystalline and less granular in the original condition, and recrystallizing from alcohol more promptly and in more definite forms.

Exposed to the air on a watch glass for 48 hours, the different parcels of this salt invariably gained slightly in weight, and this gain was fairly uniform, varying very slightly from .150 p.c. Warmed in the air to 37.7° C. or 100° F. for 48 hours more there was a slight additional gain to nearly .2 p.c. Exposed for 12 hours to temperatures between 71 and 82° C. or 160 and 180° F. it lost .550 p.c. from the original condition, and then exposed for 12 hours at ordinary temperatures it regained .100 p.c. of this loss. Up to 145° C. or 293° F. it became brownish, but remained loose in the tube and had lost 3.528 p.c. without any signs of melting. Began to melt at 152° C. or 306° F. and was entirely fused, with frothing at 156° C. or 312.8° F. with benzoin odor. Total loss on melting 6.455 p.c., and the residue was transparent and of a dark amber color.

When .4 gram. was shaken in a test tube, with successive additions of chloroform, it was not entirely dissolved when .7 c.c. of chloroform had been added, a small ring of the undissolved salt appearing against the walls of the tube at the surface of the liquid after frequent shaking during two hours. But, on standing over night, all was dissolved without any farther addition of chloroform. When to this solution three times its volume of stronger ether was added, and the whole well shaken for five minutes, the precipitated salt collected partly upon the walls of the tube and partly at the bottom, as a loose granular precipitate. But a small proportion, —enough to make the liquid opalescent,—remained in suspension, refusing to settle out completely after many days' observation. This opalescent liquid being poured off, the walls of the tube were partly covered with needle-shaped crystals in groups, and the precipitate which had settled at the bottom was covered with groups of these crystals in a crust over the precipitate. The salt first precipitated appeared to crystallize at once from the gummy, sticky condition in the tube, even before the liquid was poured off, and after drying the whole was crystallized. A repetition of this trial was necessary in order to get a perfect precipitation, and this succeeded easily after prolonged shaking, giving in the tube .4002 gram. and .076 gram., or 1.90 p.c. of residue.

The sulphuric acid test applied exactly as before described, the color became a deep red, though somewhat less deep in degree than those of the No. 1 group, and less than half the degree of some of them, but much deeper than Nos. 2 and 3.

The permanganate test was applied as in the other cases. During a few seconds the red crystals or flocks were distinctly seen mingled with the brown precipitate, before the dilution, and after dilution the liquid was a brownish-red color changing to reddish-brown in a few minutes, and after 15 minutes nearly all reddish tint had disappeared from the brown color. In an hour or two the oxide had all settled out, leaving a clear, colorless solution. A half c.c. more of the permanganate solution added to this gave the same changes, but more slowly, and on the morning following the solution was again clear and colorless. A repetition of the .5 c.c. of permanganate twice gave similar results. The salt precipitated from the chloroform solution, when submitted to this test, held the reddish color much longer,—quite as long as the similar salt precipitated from No. 2.

By the physiological test the impression was not distinguishable from that given by the standard solution, or by that of No. 2, there being no doubtful inferiority, as in the cases of Nos. 1 and 3. But it must be remembered that this test, as here applied, fails to detect with certainty known differences of 10 p.c. in strength.

The conclusions reached by these investigations were that the nine different brands or kinds of hydrochlorate of cocaine under as many different labels, which are supposed to represent a very large proportion of all that is sold in this country and, perhaps, also in Germany and in Great Britain, fall into three distinct groups. Four of the eight brands belong to the No. 1 group, and though made by four different manufacturers, are doubtless all made by stirring down a more or less pure solution during its crystallization, and continuing the stirring until the salt is more or less dry. All these salts are anhydrous in composition, and most of them contain a very small proportion of hygroscopic moisture, which is fairly uniform.

The second group is represented by No. 2. The two brands of this group are identical, and are crystallized from the concentrated solutions slowly by standing. They are, therefore, in much larger groups of much more distinct crystals. They appear to be anhydrous like the first group, but contain varying proportions of accidental water or moisture of some kind that is slowly lost by exposure to the air. As these are probably crystallized from alcohol, this moisture is probably alcoholic.

The third group also consists of two brands. These are identical and are in more or less distinct crystals, more or less effloresced, the crystals being needles, and in more or less broken up bundles, and very different from the other groups. They are also different in containing water of crystallization, which is easily varied or lost by simple exposure to air. If the published formulas of the hydrochlorate of cocaine be accepted, the anhydrous salt plus 1 molecule of water would contain about 2.69 p.c. water; with 2 molecules, 5.24 p.c.; with 3 molecules, 7.64 p.c., and with 4 molecules, 9.96 p.c. As this group lost by simple exposure various proportions in weight from 6.72 to 8.62 p.c., but in all the parcels had some effloresced crystals, it is difficult to know which of the hydrates it really is, but the probabilities are in favor of either 3 or 4 molecules. In any case it has enough to make it much the most profitable salt to make, as it is sold at about the same price as the others, but least profitable of all to use.

Now all of these brands have been very largely sold and used for all the purposes to which this substance has been applied, and all with such success that they have been in active demand and use throughout the past year. Individual preferences of one over others are often heard of, but the very few which have been inquired into by this writer, were not based upon observations accurate enough, nor definite enough to be trustworthy. Therapeutically all are without doubt of good quality, while some are excellent, and all have subserved all legitimate purposes well. The larger and finer crystalline condition of Nos. 2 and 3 and the uses made of this condition in the florid advertisements of them have doubtless had much effect in causing them to be preferred by those who do not, in establishing their preferences, go much deeper than appearances; and in this connection it is not without significance that these two forms of crystal are in successful competition at the same prices, and are very largely used when one contains an average of over 5 p.c. more water than the other; and taken together they are perhaps more popular than the first group, although this group contains, on an average, over 2.5 p.c. less water than the one, and over 7.5 p.c. less water than the other, while the chemical imperfections of the first group are considerably less than the lowest of these percentages of water. So long as good and prominent authorities are found who in the actual uses of extensive practice give decided preferences to a salt that is at least 5 p.c. weaker than others equally accessible and no more costly, it may be safe to conclude that therapeutic experience is not always a very close test of quality where the activity of agents does not vary more than 10 p.c. And this conclusion is strengthened by the results of the method of physiological testing given in this paper.

Notwithstanding that this investigation has found these nine brands to be all of good quality and well adapted to the uses of the substance, it must not be inferred that they are equally good. Four out of the eight might be considered as practically equivalent from a therapeutic point of view, and two of the remaining four as being more active than the hydrated salt. All appear to be entirely free from irritant and noxious substances, so that the question is simply one of strength, the diluent in four cases being water only, and in the other four neutral products of the splitting up of a very small proportion of the alkaloid in the processes of manufacture. And the proportion so split up is, in percentage value, and in chemical and therapeutic value also, below the diluent value of the water. That is, the hydrated salt is diluted with an average of say 8 p.c. of water which is paid for and used at the rate of the salt, while it is hardly within the limits of possibility that the inert matter in the lowest of the group of granulated crystals should exceed say 3 p.c.

In regard to the chemical character of the brands the rating is different. As chemical salts, and in chemical purity the group of two brands represented by No. 2 is the best, because it is the cleanest and best crystals, and contains less than half the amount of water, as accidental water, that the crystals of No. 3 group contain as combined water. No. 3 group rates next in chemical character, both these groups being nearly, though not quite free from the decomposition products and coloring matter of some of the No. 1 group. No. 4 rates third in chemical character, and its high therapeutic value depends on its small amount of decomposition products and very small amount of water. In common with the others of its group it possesses the important quality, for an active medicinal substance, of uniformity. Quantities weighed off from any parcel at different times will be of uniform composition and value. The other individuals of this group all rate below No. 4, both chemically and therapeutically.

The skill in making this salt of cocaine is constantly progressing, and if the time should come when the No. 2 group can be produced with only a moderate degree of loss and waste, and with less accidental or uncombined moisture, this would be the most desirable form in which to use the salt, because the therapeutical and chemical advantages would then be in accord, whilst permanency and uniformity of composition and condition would add much weight to this accordance. But so long as these crystals are obtained at so great a cost in waste of alkaloid and in time and expense of process, and so long as the granulated crystals are therapeutically equal to them, they are not necessary and scarcely desirable, especially as the difficultly crystallizable salt from which this is separated, is also put upon the market and sold side by side with it as an inferior kind.

The No. 3 group, or hydrated crystals, have the grave disadvantage for any accurate adjustment of quantity or dosage, that they are rarely twice alike, even from the same parcel. Partly effloresced in drying, they necessarily vary in the degree of efflorescence at the different times of putting up, and no ordinary skill can make their condition more uniform than that found in the different parcels examined. If the salt could be all perfectly effloresced before being put up, it would then be better than No. 2, and be best of any, because it would contain less accidental moisture than the larger crystals, and no more,—or scarcely more decomposition products; but therapeutically and chemically it would still be little better than No. 4.

It is therefore concluded that, taking everything into account, the granulated form of crystallization, when well managed, yields a product of a value at least equal to the larger and better defined crystals of No. 2 group, and it is claimed that this investigation has shown as much.

It now only remains to review the tests used in this paper, with a view to interpret them and determine their true place and value.

If there should ever be an amorphous salt in the market, the behavior under the microscope, when wetted with a fraction of a drop of alcohol, will at once detect it. A specimen which was said by the maker of it to be amorphous, and was given out as a sample of what was to be avoided in purchasing, was easily shown to disintegrate into fragments of crystals, and these, after dissolving, recrystallized in a few hours upon the slide,—remaining for a time as a sticky, varnish-like layer, by reason of the large proportion of decomposition products whose solution by drying very slowly, obstructed the crystallization. The promptness with which recrystallization occurs on the slide, and the definite form of the two kinds of crystals which successively occur during the drying, are useful indications of the freedom from decomposition products.

Exposure to air for 48 hours, simply protected from dust, is a useful indication of the amount of accidental moisture present. Only one of the group of five salts, dried by granulating the crystals, lost any weight by such exposure, and this one only lost .32 p.c.,—all the others gained in weight. The melting point was somewhat different in the different specimens, but difference in thickness of test tubes, and difference in the rate of heating up, deprive these differences of any useful significance as tests of character or quality. The odor of benzoin on fusing is characteristic so far as the writer knows.

The chloroform solubility test is, so far as he knows, original with the writer. Many authorities mention that the salt, as well as the alkaloid, is soluble in chloroform, but, so far as known, no one has published the limits of this solubility, nor its peculiar relations to this salt.

That part of the salt which crystallizes with difficulty, or does not crystallize at all, from alcohol, and the decomposition products, are much more soluble in chloroform than the easily crystallizable part, and hence greater solubility of any specimen in chloroform indicates a greater proportion of difficultly crystallizable salt, or more decomposition products, or both. Then if the chloroformic solution be precipitated by a sufficient quantity of ether, both parts of the salt are thrown down, leaving the decomposition products and a very small proportion of the salt dissolved in the chloroform and ether. Then, by drying and weighing the salt and the liquid separately, the proportion of the residue to the total salt is believed to be pretty accurately obtained. In four out of the nine cases the sum of the weights of the precipitate and residue appeared to slightly exceed the original amount of salt taken, but this was doubtless from incomplete drying, it being so difficult to dry a precipitate completely in a test tube. As there was no chance of loss excepting the loss of water or moisture, the sum of the weights should equal the original weight of salt less the moisture, and this would doubtless have been realized by more complete and accurate drying, but as all were dried alike, as nearly as possible; about the same deduction for this error must be made from all those which lose largely on exposure to air, and this correction should be something like 1.9 p.c. from the precipitate. The residue, however, is the most important element in the process, and this is not subject to any error, except that it contains a very small proportion of salt, but a proportion so small as to be nearly counterbalanced by the residue in that part of the liquid unavoidably dried upon the salt in the test-tube.

The presence of combined water in the hydrated salt renders that more soluble in chloroform, as was proved by the observation that a completely effloresced portion of this salt was much less soluble than a portion of the same salt in its original condition, and the difference in solubility was much greater than the difference in weight caused by the loss of the water. That is, .4 gram. of the effloresced salt requires 7 c.c. of chloroform for its solution, whilst the same weight in the original condition of hydration required but 5.40 c.c., yet the salt lost only 8.2 p.c. in efflorescing.

Hence, this chloroform solubility seems to be,—first, by difference in solubility, a measure of the proportion of that part of the salt which is in the condition difficultly crystallizable from alcohol; next, by the precipitation it is a measure of the total amount of anhydrous salt present that is insoluble in ether; thirdly, by the weight of the residue it is a measure of the total amount of impurities soluble in the ether and chloroform liquid; and, finally, by the loss it is a measure of the water that was present.

It is a remarkable circumstance that heating appears to have no influence either upon the rate or amount of this chloroform solubility, since if a test tube in which the salt is nearly all dissolved by standing and by shaking at common temperature, be heated in a water bath until the chloroform boils, the opalescence remains unchanged, until more chlorform be added. Then it becomes entirely transparent. The solubility appears to be also uninfluenced by cold.

The following table shows the results of this testing in compact form.

Four-tenths of a gramme of each salt taken for solubility in chloroform of s.g. not less than 1.47, and each solution precipitated by shaking with three times its volume of ether of s.g. not higher than .728.

	Chloroform required for solution.	Precipitated salt.	Residue from the evaporation of the chloroform and ether.	Sum of the weights of the salt andresidue	
No. 1..........	4.40 c.c.	.3844 grm.	.0108=2.70 p.c.	.3952 grm.	[as No. 3.
"Powdered"	6.20 "	.3864 "	.0114=2.85 "	.3978 "	Same maker
"	5.00 "	.3850 "	.0116=2.90 "	.3966 "	Same maker
H. & S..	6.50 "	.3976 "	.0100=2.50 "	.4076 "	[as No. 2.
No. 2..........	8.00 "	.4004 "	.0056=1.40 "	.4060 "	
M.........	8.00 "	.4006 "	.0052=1.30 "	.4058 "	
No. 3..........	5.40 "	.3845 "	.0114=2.85 "	.3959 "	
	5.60 "	.3840 "	.0108=2.70 "	.3948 "	
No. 4	7.00 "	.4002 "	.0076=1.90 "	.4078 "	

The best method reached of applying this chloroform solubility test is as follows :

A 40 c.c. test tube and dry cork are tared together, and into the test tube .4 gram. of the salt is put with 3 c.c. of chloroform of a s. g. not below 1.47. After a thorough shaking, it will be seen whether much or little of the salt is undissolved ; and if much then 1 c.c. more chloroform is added, and the shaking repeated. Then upon standing for half an hour a stratum or ring of undissolved salt may remain at the top of the solution, as the salt is specifically lighter than the chloroform. If this ring be small, and when shaken up only produces an opalescence in the solution, then .5 c.c. more chloroform is added and shaken, and so on with smaller additions until all is dissolved. But when the solution is so nearly effected as to leave only a slight opalescence after shaking, then if it be allowed to stand a few hours or overnight, the solution will be complete, and the liquid quite transparent. Having noted the amount of chloroform used, add three times its volume of stronger ether, s. g. .728, and shake vigorously for five or ten minutes, or until the liquid is quite transparent. At first the precipitated salt is in very fine white particles disseminated through the liquid, and the mixture is like milk. But as the shaking is continued, the precipitate begins to collect on the sides of the tube in transverse ridges or partial rings in a gummy, sticky, half-liquid condition. From some of the more soluble salts,—or from one at least,—these rings were at first transparent, and from all they were at first translucent. But gradually they become opaque as crystallization progresses, and very soon all the salt is out of the liquid, and is spread over the walls of the tube, in a half crystalline, half amorphous, sticky condition. The liquid is then poured off into a tared beaker, and the beaker, tube and cork are dried at 100° C. or 212° F. They are then closely weighed, the test tube and cork rinsed out clean, and dried at 100° C. to get a corrected or verified tare.

The results, as far as this investigation goes, may reasonably be interpreted as follows:

The larger the amount of chloroform required for solution, the larger the proportion of that part of the salt that is easily crystallizable from alcohol, and the smaller the proportion of products of decomposition. But .4 gram. of this part of the salt, when as free from the other, and as free from decomposition products as practicable, is perfectly soluble in 9 c.c. of chloroform.

The weight of the precipitate, if perfectly dried, represents the total amount of salt present, embracing both conditions.

The weight of the residue closely represents, but rather exceeds, the total proportion of decomposition products and other impurities soluble in the chloroform and ether. And this residue is believed to be a fair indication of the therapeutic value of the anhydrous salt, but not of the hydrated salt.

The sum of the weights of the precipitate and residue, subtracted from the weight of salt originally taken, give the loss in the process, and this may safely be interpreted as water or moisture present in the original salt.

When the salt to be submitted to this test is in the larger crystals, as the group No. 2, it is very difficultly soluble in the smallest proportion of chloroform that will dissolve it, unless it be very finely powdered before being weighed off, and in this powdering almost all the moisture, whether of alcohol or water, that was accidentally held in the intercrystalline spaces,—goes off and leaves the final results that much better than they really should be.

The chief inconveniences of this chloroform test are, first, that it requires accurate and close weighing and measuring. But this can be measurably overcome by multiplying the quantities taken; and this involves no loss, because the precipitated salt is better than the original salt, and being closely weighed it can be at once converted into 4 p.c. solution, and be added to the stock of solution.

Next, the solution requires considerable time and agitation in reaching the point of solubility, and the point is often overreached, and a new portion must then be taken if accuracy be particularly desired. Next, it is very tedious and difficult to dry the precipitate in the test tube, and impracticable to take it out for drying.

In a rather rough, or not very critical way, however, it is very easily applied, and in such application often need be carried no further than to determine that .4 gram. of any specimen is not soluble in less than a given amount of chloroform, though this does not determine therapeutic efficacy, but only chemical character. The test, as a whole, is, however, more useful than any one known to the writer.

The test of Dr. F. Giesel, by solution of permanganate of potassium, is hypercritical and often fallacious. It fairly discriminates the chemical character of the salt, but is of little or no value as indicating therapeutic efficacy or value. The violet-colored acicular crystals, described by Dr. Giesel, are sometimes seen and sometimes not, even with the same salt. Rose-red flocculi are, however, generally seen before the dilution, but these are probably oxide of manganese colored by the solution. The best and purest salt that could be made, when subjected to this test, gave a solution that retained some red tint in the brown for two hours or more. But the next day it was colorless and transparent, with a deposit of oxide at the bottom. Another portion of permanganate solution added to this, again went through similar changes, and again the liquid became colorless. This is supposed to prove that the salt itself, however pure, is split up by the permanganate,—and it would be very remarkable if so very sensitive an alkaloid did resist such action. From this circumstance, and from the very different reaction of the test upon specimens of equal therapeutic value, it is inferred that the permanganate first attacks that part of the salt which is so loose in composition as to be difficultly crystallizable. If the proportion of the salt which is in this condition be small, all the permanganate is not decomposed at once, and the red color continues for a slower action upon that part of the salt which is easily crystallizable. But if the proportion be large all of the very small amount of permanganate is decomposed at once, and no red color is seen after the moment of mixing. These market specimens gave almost every degree of variation between these extremes, and yet it is believed, upon fairly good evidence, that there was not a really bad specimen of the salt among those examined. Indeed, if a critical application of this test, wherein the red-brown color should be retained at the end of an hour, be insisted upon, seven of the nine brands would be rejected, for it has been shown that the two specimens of the No. 2 group alone withstood this test. But as it has been shown that none of the seven were really bad, and that two or three of these, at least, were of equal value with No. 2, this test must be considered fallacious, and, if fallacious, then practically useless,—as useless here as it would be with a very large number of important alkaloids and their salts.

The sulphuric acid test is also of doubtful utility as applied to this salt at the present time. Should it ever become practicable to make a chemically perfect salt, in large quantities, without very great waste and loss by decomposition, and should it be shown that such a salt was more active, then such tests as this and the preceding one would be very valuable. With the exception of a standard sample made for the purpose, no parcel tried gave a perfectly colorless liquid. The acid decomposes the salt at once with effervesence and a strong, chlorinous odor, and the color of the resulting liquid depends upon the varying conditions of this decomposition and the more or less coloring matter present. In some instances where there was least color the salt was doubtless the best, but this was not uniformly the case, nor was the greatest color indicative of the worst salt. Indeed, the color developed seemed to be proportionate to the coloring matter left in the salt, and it is well known how small a trace of coloring matter affects sulphuric acid.

The physiological testing as here practiced does not discriminate closely enough, and if it did, it would not be of practical applicability in any general way, because people in general are so very differently sensitive to very delicate impressions on the tongue. Faithfully applied it is laborious, and requires much time and care, and an education of those whe are to be used in applying it. Nevertheless, it has proved very serviceable to the writer in supporting other evidences.

The test by litmus paper of the acidity of strong solutions is very easy of application, and the writer is inclined to consider it of much importance, when skillfully and critically applied.

Cocaine completely saturates hydrochloric acid, and solutions, however strong when freshly made, are absolutely neutral to the most sensitive test paper. But solutions from salts that have been some time made, are invariably faintly acid, and appear to vary in their acidity in proportion to the moisture they contain. That is, the dryer the salt that has thus been kept for some time, the more faintly acid the solution made from it.

This taken in connection with an important fact stated by Prof. Fluckiger long ago, that solution of hydrochlorate of cocaine cannot be evaporated without decomposition,—leads the writer to the inference that this acidity is due to a slight decomposition of the salt wherein the base is destroyed and the acid set free,—and that this decomposition is due to the presence of water; and finally, that the more water there is present the more salt will be decomposed spontaneously by time, and therefore the more acidity. Why the water present in the anhydrous salt does not combine to form the hydrated salt is among the very many things still unknown in regard to this very singular alkaloid and its salts.

To this may be added the conviction from the writer's experience that not only does water determine a slight, slow decomposition of both the alkaloid and salt, but that every process to which they are subjected,—every solution,—every precipitation,—every handling, and even every long exposure to the atmospheric vicissitudes of dryness and moisture, determine a slight decomposition, and that, therefore, all chemical torturing to improve the mere outside appearance of the salt is to be deprecated as being injurious to its therapeutical efficacy.

MINIM PIPETTES.

In the course of a paper upon the administration of medicines published in these pamphlets at page 837, there is a cut and a description of a set of minim pipettes at page 844, which attracted the attention of Mr. A. C. Abraham, one of the well-known pharmacists of that long-established name in Liverpool. Mr. Abraham courteously mentions to the writer that his father described a similar instrument prior to 1851, and refers to the description as published in "The Pharmaceutical Journal and Transactions," 1st Series, Vol. IX., page 171, and Vol. XI., page 268.

It gives the writer pleasure to publish this acknowledgment of the priority of Mr. John Abraham, of Liverpool, to any credit or utility there may be in this device. The writer's set of "The Pharmaceutical Journal" only goes back to 1858, and he has never seen, nor before heard of the papers above referred to, and therefore wrote his paper in entire ignorance of what had been done by Mr. Abraham. The minim pipette was offered by the writer not as an invention, but merely as a convenient and simple device, without any claim to either novelty or originality, but had he known of Mr. Abraham's papers it would have been most agreeable to have referred to them with due credit and thanks for the great benefit derived from the use of the pipettes. Their utility is such, that, as Mr. A. C. Abraham remarks, it is singular that they are not more generally used when there has never been a patent, or restriction of any kind upon making or using them, and when any pharmacist can, if he wants them, make them for himself.

It seems to be only an illustration that many pharmacists,— and many teachers of pharmacists, cling with tenacity to old customs and habits of their art, and seem to neither know nor care for the progress they need unless they are advertised into it in some catchpenny way.

THE PHARMACOPŒIA OF 1880.

(Review Continued.)

EXTRACTUM OPII.

EXTRACT OF OPIUM.

Opium, *one hundred parts*	100
Water, *seven hundred and fifty parts*	750
Glycerin, *a sufficient quantity*	

Cut the Opium into small pieces, let it macerate for twenty-four hours in *one hundred and fifty* (150) *parts* of the Water, and reduce it to a soft mass by trituration. Express the liquid from it, and treat the residue again in the same manner with *one hundred and fifty* (150) *parts* of the Water. Repeat the maceration and expression three times more, using a fresh portion of the Water each time. Having mixed the liquids, filter the mixture, and evaporate, by means of a water-bath, to a pilular consistence. Lastly, weigh the Extract and thoroughly incorporate with it, while still warm, *five* (5) *per cent.* of Glycerin.

Preparations: Emplastrum Opii. Trochisci Glycyrrhizæ et Opii.

This preparation is very variable from several causes, but chiefly because no two parcels of opium yield the same amount of extract even under the same management,—whilst under different management the same opium will give different proportions of extract, and when the proportion of extract varies, the strength of the extract will vary of course. It varies also in consequence of the antagonism between the commercial and the therapeutic interests involved. The manufacturer, of course, wants to get the largest proportion of extract from the opium, which means a feeble preparation, while the interest of the therapeutist is to have the smallest proportion of extract, because it will be then stronger and more free from those elements, which give the extract the advantage over opium. While the management by the officinal process yields about the largest proportion of extract obtainable from opium, it, therefore, yields the feeblest, but it has the advantage that no ordinary commercial management can yield a larger proportion or a more feeble extract. Authorities vary very much in the proportion of extract which opium should yield. Under the title "Opium" the Pharmacopœia says: "On exhausting 100 parts of opium, previously dried at a temperature of 105° C. (221° F.) with cold water, and evaporating the solution to dryness, an extract is obtained, which should weigh between 55 and 60 parts." The writer's experience leads to the belief that this proportion is considerably understated, and all accurate experiments made for the purposes of this paper show that two different powdered opiums,—one containing 13 and the other 16 p.c. of morphine, and each powder containing between 3 and 4 p.c. of moisture, which was lost at 105° C.,—gave of dry extract, the one 64.375 p.c. and the other 63.532 p. c. These results calculated back to a powder dried at 105° C. would give the corrected results at about 67 and 66 p.c. of dry extract,—and of pilular extract made by the above process of the Pharmacopœia about 75 and 74 p.c. Then, as there is a loss of about .5 p.c. of morphine in the process, the dried extract would contain respectively about 19.7 and 24.7 p. c. of morphine, and the moist extracts about 18.9 and 23.7 p.c.

To illustrate the practice with this extract the following trials were made: Half a pound of good commercial Smyrna Opium was bought in the market, and treated by the officinal process as closely as practicable. The yield of moist pilular extract was 59.55 p.c., but it might easily have varied 1 or 2 p.c. either way in judging of the proper pilular consistence.

The prominent criticisms on this process are as follows:

Moist opium, in the commercial condition, is directed by the Pharmacopœia. This is an important mistake, for the following reasons: The average morphine strength of opium is never attained by taking any given lump or lumps of moist opium, while an average morphine strength and an average amount of water are both secured by taking powdered opium, and thus much greater uniformity of results are attained. Again, in the drying out and powdering of opium a small but not unimportant proportion of the inert or objectionable organic matter of the crude drug is oxidized or otherwise changed from a soluble to an insoluble condition, and is thus excluded from the extract. And, finally, powdered opium is more easily and more completely exhausted by ordinary management. All these circumstances have long been well known, whilst any one of the causes is sufficient to decide as between the use of moist and powdered opium for making the extract.

When opium is macerated for 24 hours with any proportion of water less than five or six times its weight, the solution will precipitate on the further addition of water, or of weak solution, and the precipitate is so fine and so glutinous that it is very difficult to filter out; and, under all circumstances, involves another filtration, or about 24 hours to settle out, this latter being the best way to get it out. When it settles out it forms a sticky black layer on the bottom of the vessel, which should be excluded from the extract, but which the Pharmacopœia does not exclude. If the opium be macerated for 12 hours, with occasional agitation, with ten times its weight of water, a perfectly clear solution is obtained, which does not precipitate under the conditions above mentioned, and this solution contains fully 95 p.c. of the extract. It is best managed by filtration through a double paper filter, percolating the residue upon the filter with water to about the weight of the opium. The direction to express this residue is objectionable, because it contains enough caoutchouc-like matter to prevent a moderate degree of success, and it is a sticky, troublesome process, which so compacts the residue as to obstruct farther exhaustion. It is much better to keep the residue as loose as possible. After being once percolated it should be returned to the vessel and be well agitated with water in the proportion of about twice the weight of the opium. Two or three hours' maceration, with occasional agitation, is thus sufficient, when it is returned to the same filter and drained. Finally, it is percolated with about the same quantity of water as before, and is thus practically exhausted. A little less morphine is lost by evaporating the weak liquids first, because then the stronger solution is exposed to heat for a shorter time.

The direction to evaporate to a pilular consistence is hard to follow out, and is much too indefinite in modern pharmacy, especially with a preparation which contains about 20 p.c. of so potent an agent as morphine. But the other alternative, to evaporate to a given weight, is impracticable in the case of a drug which varies so much in its proportion of water and other useless constituents.

As this is one of the extracts that can be very safely and very easily evaporated to brittleness when cold, and be then powdered, this is by far the best practice with it. And the finished powder should always be assayed, and the assay given on the label.

No arguments can be needed at this day for having extracts in powder rather than in mass, where the former condition is practicable without foreign admixture, and certainly none for having potent extracts assayed. But it would be well for pharmacopœial authority here, as in Great Britain and Germany, to require a definite strength for the extract. The British Pharmacopœia requires "about twenty per cent." of morphine, and the German not less than 14.6 p.c. Both these authorities wisely direct the extract to be made from powdered opium, but how the first expects to get a 20 p.c. extract from its officinal opium of not less than 9.5 nor more than 10.5 p. c. of morphine, is not easy to comprehend.* A very good standard of strength for the extract would be 20 p.c., but, as will be presently shown, this requires a powdered opium of not less than 13 p.c., and this is, perhaps, a little above the average strength of the powdered opium of the market. It is, however, always easy to get a higher grade of powdered opium at a proportionately higher cost, and an extract from such could be easily reduced to a standard strength by dilution with powdered sugar of milk.

The following experiments were made to illustrate the above mentioned points :

Took 5 ounces avoirdupois, or 141.75 grammes of powdered opium containing by assay 16 p.c. of morphine, and digested it for 12 hours with 10 times its weight of water in a wide-mouth bottle, agitating frequently. Drained the residue on a double paper filter, percolating it with about 150 c.c. of water. Then returned the residue to the bottle and shook it well with 300 c.c. of water, and again filtered off the solution and percolated the residue as before. Again returned it to the bottle and repeated the shaking with 150 c.c. water, and the filtration and percolation. Evaporated the filtrates in a tared basin on a water bath, beginning with the weakest, and adding one fraction after the other, until the extract appeared to be of a proper consistence. It then weighed 97 grammes, and to this was added 5 p.c. or 4.9 grammes of glycerin, and the whole was well stirred together. The finished extract then weighed 101.5 grammes, or 3½ ounces and 35 grains, or 71.6 p.c. of the powdered opium. Now the 141.75 grammes of powdered opium of 16 p.c. would give a total of 22.68 grammes of morphine in the 101.5 grammes of finished extract, or 22.34 + p.c., provided there was no loss of morphine in the process. But upon assaying the extract it was found to contain only 21.82 p.c., and therefore the loss of morphine split up in the process was .52 p.c.

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*It is very remarkable that these two of the most modern of the Pharmacopœias should have used their influence to debase the quality of opium. There is no unadulterated opium in this market, nor in any other known locality, Persian opium alone excepted, which, when dried and powdered, will yield as little as 9.5 to 10.5 p.c. of morphine. As commercial opium, on an average, loses about 20 p.c. in drying for powdering, a powder which gives 9.5 p.c. would indicate that the opium, in its moist commercial condition, contained only 7.6 p.c. of morphine.

Then took the same quantity of the same powdered opium, and treated it in exactly the same way, excepting that the extract was evaporated to dryness without the glycerin, and the dry extract was rubbed into fine powder.

The yield of powdered extract was 62.3 p.c. of the opium, and had there been no loss of morphine in the process it should have contained 25.6 p.c. of morphine. But by assay it yielded only 25.12 p.c., showing a loss of .48 p.c.

A comparison of these results shows that from the same powdered opium the difference between the officinal extract and a powdered extract is 9.3 p.c. in weight, and 3.3 p c. in morphine strength,—commercially very much in favor of the officinal extract of pilular consistence, but pharmaceutically very much in favor of the powdered extract, because it is so much more easy to weigh off accurately in prescriptions, and to keep in a uniform condition without loss or inconvenience; while, therapeutically, the powder is much better, because it is stronger; more uniform and more accurate for dosage.

In re-dissolving these extracts in cold water for the assay process, it was found that that from commercial opium in its moist condition, as taken by the Pharmacopœia, leaves an insoluble residue of 6.25 p.c., and that from the powdered opium 4.53 p.c., showing a difference of 1.72 p.c. of objectionable extractive matter excluded by the use of powdered opium.

Next 20 lbs. of powdered Tokat opium containing 13 p.c. of morphine was taken and made into powdered extract in exactly the same way. The opium, in its moist commercial condition as received, contained 10.91 p.c of morphine, and it lost in drying and powdering the unusually small proportion of 16.1 p.c. of moisture. This powdered opium yielded 64.375 p.c. of powdered extract, and this powder should have contained 20.2 p.c. of morphine, but upon assay it was found to yield only 19.6 p.c., showing a loss in manipulation of .6 p.c.

The insoluble residue in the extract from this opium was 9.3 p.c. of the extract.

The principal therapeutic advantages of extract of opium over powdered opium are first that by the extraction with cold water many of the constituents of opium, which tend to produce nausea and headache from its use, are excluded wholly or in greater part. Next, if in powder, it is more than one-third stronger in morphine than the opium from which it is made, and from its smaller bulk it is peculiarly and specially adapted to combination with other remedies in pills and powders; and finally, that its therapeutic effects are those of opium, and not those of the salts of morphine.

The dose will vary very much with the quality of the opium from which it is made, and of course with the special object for which it is used. Two parts of the extract are about equal to three parts of the opium from which it is made, but as the Pharmacopœia has no maximum limit for opium, and admits of a variation of 4 p.c. of morphine strength in its powdered opium, which is equal to 33 p.c. on its minimum of 12 p.c. and 25 p.c. on its maximum of 16 p.c., and as this variation is largely increased in the extract, the dosage is very much confused. As a general statement, however, the dose is about one-third less than of powdered opium.

It is a very convenient preparation for external or dermic use, and for such purposes is too much neglected or overlooked. Moistened with water to a semi-liquid consistence and spread very thinly upon oiled silk or upon adhesive plaster, leaving a margin for adhesion to the skin, it makes a very efficient application for the relief of local pain, while it saves the general economy from a large proportion of the disturbance caused by the use of opiates by the stomach or hypodermically, because, the effect is produced at the point affected, and does not have to be reached by the much larger quantity required to impress the whole organism.

TESTING ACONITINE.

If $\frac{1}{8000}$ of a grain of aconitine be dissolved in a fluidrachm or 3.75 c.c. of distilled water, and the solution be held for one minute in the anterior part of the mouth, and be then discharged, a distinct aconite impression will be noticed within 15 minutes, and will last for an hour or two. The impression or sensation can hardly be described, and a description need not be attempted. Sufficient to call it a feeble but distinct aconite impression, since it is not difficult to recognize when watched for. A convenient way of making the solution for testing is to weigh off half a grain, or 32.5 millegrammes of the aconitine, add a little distilled water and about .2 c.c. of acetic acid, and stir until it is dissolved. Then make the solution up to 100 c.c., or 3⅓ f ℥, with distilled water, and mix well. Of this solution, one-tenth of a cubic centimetre, made up to 60 minims or 3.75 c.c., with distilled water, is the dose for testing.

When the aconitine is of good quality a distinct impression will be noticed in any ordinarily sensitive mouth which has been rinsed out just before receiving the dose. But many of the aconitines of the market will give no impression from one-tenth of a cubic centimetre. Then after waiting an hour double the quantity, or two-tenths of a cubic centimetre, made up to 1 f ʒ, should be tried in the same way. This quantity is equal to $\frac{1}{1000}$ grain, and should this give no impression the quantity may be doubled again,—and so on until an impression be obtained.

The dilute solutions lose their strength very rapidly on standing, and more rapidly in warm weather than in cold, and the testings should always be made within 24 hours after the solutions are made, since in 48 hours they have sometimes been found inert, or very nearly so.

In some recent trials the aconitine of Duquesnel, of Paris, and aconitine made in the writer's laboratory from the root of aconitum napellus, gave nearly equal and very distinct impressions from one-tenth of a cubic centimetre, equal to $\frac{1}{2000}$ of a grain.

As the test, when carefully applied, will usefully, if not accurately, ascertain the strength of any parcel of the alkaloid, and as much of that of the market is very feeble, none should be trusted in medicine which has not been tested. Then, if by testing, a definite strength is ascertained for any given parcel, the physician may, by adjusting the dose to the strength, use a more feeble alkaloid in larger quantity with the expectation of similar results. But, certainly, large doses should never be used, under any circumstances, without having been preceded by smaller ones at proper intervals without effect, and the use of each new parcel of the alkaloid should be commenced on the assumption that it is of the greatest normal strength, as indicated by the testing, because, as a poison, this alkaloid is very rapid and deadly in its action.

In view of its great variability and potency it is not well adapted to the ordinary uses in medicine wherein aconite is so important, and therefore the alkaloid should be reserved for special uses, and the fluid extract of the root be applied to the common uses.

TESTING FLUID EXTRACT OF ACONITE.—(ROOT.)

One-fifteenth of a minim of a well-made fluid extract of Aconite Root, made from good root, by repercolation, and representing the root in the proportion of minim for grain,—in a fluidrachm of water, will give a very faint, but still fairly distinct aconite impression if held in the mouth for one minute. One-tenth of a minim in a fluidrachm of water gives a very distinct and much stronger impression, lasting generally for an hour or two. A good way of applying the test is to add 10 minims or .616 c.c. of the fluid extract to 12.5 fluidounces or 100 fluidrachms, or 369 c.c. of water, and agitate them well together. Each fluidrachm of this solution represents one-tenth of a minim. If the mouth be well rinsed out with water, and this quantity be held in the anterior part, around the end of the tongue, for one minute by the watch, and be then discharged, a distinct, definite and characteristic aconite impression is easily perceived. From one-tenth of a minim the impression is so strong at the end of ten or fifteen minutes that it is not easily missed.

If the solution be made one-half weaker,—that is ten minims in eighteen and three-quarter fluidounces or 150 fluidrachms, so that each fluidrachm represents one-fifteenth of a minim of the fluid extract, then the impression from a fluidrachm of this is so faint that unless it be watched for it is not always noticed. But if watched for it is generally perceptible in fifteen or twenty minutes, and is stronger or weaker at intervals for half an hour, and then disappears.

This is about the limit of the test for a good fluid extract of full officinal strength, and no fluid extract should be accepted which does not give a distinct impression from one-tenth of a minim.

The Fluid Extracts of Aconite of three of the most prominent and largest makers for this market were carefully submitted to this test, with the following results:

The first is made with alcohol, and the label states that each minim represents ninety-five hundredths of a grain of Aconite Root. But on application of the above test no aconite impression was obtained. A stronger solution was then made, one-seventh of a minim in the f ʒ of water, but still no distinct impression was obtained. Then a solution of one-fifth of a minim to the f ʒ was tried, and this gave a faint but distinct impression to two out of three persons who tried it. This preparation was therefore not more than half the standard strength, and therefore if used in the standard dose of one to two minims, as given on the label, it could not yield the standard results.

The second bottle was also made with alcohol as a menstruum, and was described on the label as being of the standard strength of the U. S. Pharmacopœia of 1880, and the dose as being one minim or less to five minims. This preparation failed to give a distinct impression until the f ʒ of water contained three-tenths of a minim, and it was, therefore, about one-third of the standard strength, and three to six minims would be the standard dose.

The third specimen was made with Diluted Alcohol* as a menstruum, and was described on the label as of the strength of a minim for each grain of aconite root. This preparation responded fully to the standard of the test. The cost of these fluid extracts was, respectively, $0.96, $1.20 and $1.31 per pound in quarter pound bottles, with discounts off. The first two must have been either very carelessly made or made from root of an inferior quality.

Now, as $\frac{1}{2000}$ grain of good aconitine gives an impression, which is approximately equal to that from one-tenth of a minim of good Fluid Extract of Aconite Root, it follows that this tenth of a minim should contain approximately $\frac{1}{2000}$ of a grain of aconitine. Then a minim should contain $\frac{1}{200}$ of a grain, and two minims should contain $\frac{1}{100}$ of a grain, and this gives practically the equivalent doses of the alkaloid and fluid extract when both are of standard quality. From this equivalency it would seem that good aconite root contains $\frac{1}{200}$ of its weight or .5 p.c. of aconitine, but this is some six or seven times as much as is given by the best authorities, and more than three times as much as the writer has obtained under very favorable conditions. This discrepancy is at present without rational explanation, since it appears improbable that two-thirds of the alkaloid, or more, should be destroyed in the process of extraction.

In this connection it seems worth while to attract especial attention again to the rapidity with which dilute solutions of the salts of the strongest aconitine become inert. It has repeatedly occurred to the writer to find dilute solutions of the acetate of aconitine become entirely inert by standing 48 hours in closed vessels, and yet give no signs of the growth of mycelium to the naked eye. The quantity of alkaloid is, however, so very minute that growths sufficient to destroy it would be microscopic.

This whole subject of aconite and aconitine is treated of at much greater length at page 123 *et seq.*, of this series of pamphlets, but as it seems to have attracted much less attention than the importance of the subject deserves, it may not be amiss to have returned to it with the results of accumulated experience, particularly when it is remembered that preparations of aconite are among the most prominent and definite articles of the modern materia medica, and becoming more important every day.

THE ALCOHOL QUESTION BEFORE CONGRESS.

The important subject of the internal revenue tax is again to be brought up in Congress, and embracing as it does the tax on alcohol or spirit in all its forms, it is of great interest in medicine and pharmacy.

More than two years ago, when it was last before Congress, this writer made some investigations upon the subject, and the conclusions were published in these pamphlets at page 494.

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* The Pharmacopœia requires stronger alcohol, but this is a mistake. Diluted Alcohol exhausts the root quite as well as any stronger menstruum, and has the great advantage of yielding a preparation which does not precipitate on being added to water, and it is an excellent as well as an almost universal practice to administer aconite preparations diluted at the time, so that a given teaspoon shall measure the desired minims or fractions of a minim in the teaspoonful of water.

All the conclusions then reached have been much strengthened since that time, and it seems more plain now than ever that if Congress will only investigate the subject thoroughly it will again take the ground that if the tax on spirit cannot be totally abolished, it should not be touched in any way. It is simply a question of finance. As soon as the financial condition of the country will permit it there is probably nothing that will relieve more of the small and struggling industries of the nation, nor foster more new ones than the abolition of this spirit tax. Any discrimination by which to relieve these industries without relieving the spirit used in beverages will, in this country, surely fail to relieve the law-abiding manufacturer, but will relieve the unscrupulous and evasive.

The form of discrimination which again appears popular with legislators, is, by means of a methylated spirit, to be exempt from taxation. The last time this was proposed it was combatted on the ground that such a spirit could be easily cleaned, but it is now reported that Washington chemists find, upon careful investigation, that such a spirit cannot be cleaned so as to fit it for any clean uses. If this were true, such spirit could not be honestly used for any cleanly purposes, and therefore all manufacturers who use spirit for clean purposes would not be relieved by this device, but would be subjected to a ruinous and unfair competition with such as would use it when they ought not. But the statement is not true, for methylated spirit can be cleaned, and for all the proper uses of it by a very large proportion of manufacturers, they must be allowed to clean it for themselves, for if not, the discrimination is no relief to them. The proposition, however, is to prohibit the cleaning of it under heavy penalties,—and this would seem to be necessary or it would all be cleaned and go into beverages, and none be left to pay the tax. But if it cannot be cleaned, as legislators seem to believe, why prohibit the cleaning? The practical working of a methylated spirit law is to permit those who most need relief by it to clean it for themselves, and to prevent all others from cleaning it, and this cannot be done under this form of government.

If the honest consumer of spirit in this country is to have as fair a chance of profit from its use as the dishonest one, the tax must be applied without discrimination of any kind.

The next most popular form of relief seems to be a uniform reduction of the tax, and this is far better than any form of discrimination. But it must be the policy of the Government to relieve the people entirely from this tax as soon as possible, leaving it with the States to control their interests in the beverage part of the business, as they do at present by a duplicate machinery. The Government undoubtedly sees that the immense natural resources involved in spirit manufacture can only be developed under an entire abolition of this tax. With the vast area, and the soil and climate of this country, the extent and profit of grain production can hardly be equaled. The conversion of the surplussage of this grain into spirit by the improved and still improving processes now used, embraces the production of sound and healthy beef and pork through a corrected and intelligent use of distillery residue as an important part of the food for stock, and thus the two enormous elements of spirit and meat production are joined in one industry. With this industry entirely untrammeled its products should and would go all over the world at a large profit to the nation.

The false political economy of this tax is seen in another way.

A statement recently published, and said to be compiled from official statistics, shows that the people of this nation pay annually $900,000,000.00 for the spirit consumed, while for bread and meat together they pay $808,000,000.00. As spirit is taxed to about eight times the cost of production, and about seven times its market value, the people are paying for their largest national expenditure over seven times its value. With spirit untaxed, and the same profits to those who sell it to the people, it would only cost them $150,000,000.00. But the Government does not get the other $750,000,000.00 now, but spends a very large proportion of it upon two classes of middle men, who come between the producer and consumer. The first of these is the army of office-holders necessary to collect the tax, and next the still more numerous army of licensed liquor dealers. And these two classes, thus supported by this tax, are mainly used against the people so far as their efforts and their votes can go in keeping the political party which supports them, in power, and keeping all others out. If the tax be abolished, these two classes will be disbanded and lose their support, and thus the Government would gain in reduced expenses a very large proportion of what it would lose in revenue from this very expensive tax. But in losing the control of many thousand votes and several millions of money, a reason may be found as to why the Government will never advocate the abolition of this tax. It may consent to a reduction of the tax, or to any scheme which will not too much reduce its army of voters, and the money necessary to watch and collect the tax, because it takes as many officials and as much money to collect a small tax as a large one. But to relinquish the votes and the money is perhaps too much to expect of any political party in power; and as the party out of power always hopes to get in, it is also too much to expect from that. It is not, however, too much to expect that the Congress will rise above these party interests and strife and enforce a more true political economy. Abolish the tax and this largest national expenditure will be reduced to the second or third in rank, and leave another narcotic luxury at the head of the list, namely, tobacco. It has been said that tobacco is the poor man's solace, and is among his few necessities, and therefore should be first freed from tax. But spirit in some form is hardly less his solace, while it is actually an inferior form of food to his organism, while tobacco is not.

In this connection it is curious to reflect that the two elements of highest cost of human life, as it is lived in the aggregate, are spirits and tobacco, the one a stimulant narcotic, the other a depressant narcotic,—and that more than one-third of the human race prove by living without them that they are in no degree necessary nor healthful, but on the contrary tend to depravity and destruction.

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Vol. III. No. 2.

AN EPHEMERIS OF MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

OCTOBER, 1887.

BY
EDWARD R. SQUIBB, M. D.
EDWARD H. SQUIBB, S. B., M. D.
CHARLES F. SQUIBB, A. B.

BROOKLYN, N. Y.
1887.

NOTICE.

The number of applications for these pamphlets have been unexpectedly large, and most persons have wanted the back numbers: many also have lost back numbers who wanted to file them, and have had to write for duplicates. Some at first were supplied free of cost, but several numbers of each volume have had to be reprinted at considerable additional expense, and therefore all future applicants will be asked to pay for them.

Because of the time and postage required in answering letters, neither the pamphlets, nor a reply and explanation need be expected unless the price of the numbers desired be sent with the application for them.

For each back number desired the sum of ten cents must be remitted with the application, in postage stamps or by postal note, this sum covering the cost and postage on each number applied for.

The two complete volumes are still accessible to all those who want them, bound separately in cloth. They will be sent free of postage for $1.16 each.

AN EPHEMERIS

OF

MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

VOL. III. OCTOBER, 1887. No. 2.

Many who receive these pamphlets do not appear to understand that they are no longer published with regularity, and may cease to be published altogether at any time, and the correspondence necessary to explain why they are not sent regularly, or more frequently, takes up much valuable time, which would be better given to the pamphlets in another way. Although it is rather discourteous not to reply to letters, especially when stamps for replies are enclosed, the readers of these pamphlets will please understand that anything like discourtesy is distinctly disclaimed, when in future such letters are not answered.

Only one number of the series has been published this year,—in January,—and this one in October is the second ; and this one may be the last ever published. The January number was mailed to every name on our directory ; and to many names, whose addresses had been changed without notice, a second copy was mailed on request. The same course will be taken with this number, but no responsibility is accepted, nor any promise implied for the future. Should there be any more issues in the future, they will be freely distributed, as in the past, to every name now on the directory, and to every name that may request to be put on the directory, but it is by no means certain that another number will ever be published. Therefore future numbers should not be written for with the expectation that the writer has the time at command to reply to all such letters.

THE OIL OF WINTERGREEN (OIL OF BIRCH) AS A THERAPEUTIC AGENT.

BY EDWARD R. SQUIBB, M. D.*

Subsequent to the use of salicin and its derivatives in rheumatic affections, and prior to 1882, Mr. P. Casamajor, the well known chemist of Brooklyn, reasoning upon purely chemical data, had used on his own person, and upon several friends, the oil of wintergreen as an effective salicylate with good results in some rheumatic affections. These results he communicated to this writer. As well trained chemists usually reason closely and accurately, and are careful observers of the relations between cause and effect, the results of Mr. Casamajor's observations impressed this writer strongly, and resulted in the first published statement of the use of this oil as a therapeutic agent in the EPHEMERIS for January, 1882, page 30. The use of oil of wintergreen by Mr. Casamajor was not an empirical trial of an essential oil to see, perchance, if it might not "be good for rheumatism," but being acquainted with the reputation of salicin, salicylic acid and the salicylates, and of some of the disadvantages of their use, and knowing that oil of wintergreen consisted chiefly of salicylic acid and methyl in combination loose enough to be more easily effective than the other salicylates which had been used up to that time, he applied it with success.

He therefore had tried oil of wintergreen, not as an essential oil, but as methyl salicylate, upon the rational expectation that this combination of the radicle salicyl would prove to possess some advantages over the combinations hitherto used. To him it was not so much oil of wintergreen as it was methyl salicylate, or methyl salicylic acid, or methyl salicylic ether, and had he known that he was probably not using oil of wintergreen at all, but oil of birch sold under that name, it would have made no difference to him so long as both oils were alike in consisting mainly of methyl salicylate.

The note published in the EPHEMERIS of January, 1882, soon attracted the attention of physicians, and it was not long before the oil was in use upon a scale sufficiently large to be the basis of more definite conclusions.

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* Read before the Kings County Medical Association at the stated meeting' held April 5. 1887.

The first paper noticed was by Dr. Francis P. Kinnicutt, who reported some seventeen cases in all, closely observed in St. Luke's Hospital. This paper was read before the Practitioners' Society of New York in October, 1882, and published in The Medical Record of New York, vol. XXII., No. 19, page 505. From that time to the present, reports of cases, and notices of its use have occasionally appeared in the journals, and all these, so far as observed by this writer, have been favorable to its use.

The attention to the agent thus aroused has doubtless within the past four years led to its frequent application by many observers, and it is one of the objects of this paper to bring out some expression of the local experience with the agent in Brooklyn, where it was first used, and where it has probably been most used.

Another object of this paper is to give a brief history of the agent, and to correct some prevalent errors in regard to the name and sources of supply, in the interest of greater accuracy, as the substance becomes more important in the materia medica.

Some time prior to 1839, Pagenstecher obtained a volatile oil by distillation of the flowers of Spiræa ulmaria or Meadow Sweet, with water, in which oil Löwig and Weidmann recognized a hydracid of much chemical interest.

In 1839 Piria discovered a hydruret of salicyle as a product of the decomposition of salicin, and soon after Ettling demonstrated the identity of the hydracid of Löwig with the hydruret of Piria, which the latter called salicyle. From or upon this radicle, salicylous and salicylic acids are formed. These derived their name from the salicin of willow bark, but were the same, in both physical and chemical properties, whether obtained from Meadow Sweet or from willow bark.

After these investigations it was for some years suspected, chiefly from a similarity of odor between the oils of Spiræa ulmaria and Gaultheria procumbens or wintergreen, that the latter oil was of the same construction or composition as the former, but up to 1842 no steps were taken to investigate this supposed identity of structure. In October, 1842, Prof. William Procter, Jr., of Philadelphia, published in The American Journal of Pharmacy, vol. XIV., or New Series, vol. VIII., p. 211, a paper entitled, "Observations on the Volatile Oil of Gaultheria procumbens, proving it to be a hydracid analogous to Salicylous Acid." In this paper Prof. Proctor appears to have obtained salicylic acid, but without distinctly recognizing it as such.

From this and a subsequent paper by the same author, and from Gmelin's Hand-Book of Chemistry, much of this information is taken.

Next Cahours took up the investigation, and in a paper published in the Journal de Pharm. et de Chim. of May, 1843, proved that by the distillation of salicylic acid with pyroxylic spirit and sulphuric acid a product was obtained having the properties and constitution of the oil of wintergreen, thus showing synthetically what had before been shown analytically.

Next Prof. Procter in a second paper published in The American Journal of Pharmacy for January, 1844, vol. XV., or New Series vol. IX., p. 241, shows that oil of wintergreen is identical with a volatile oil obtained by distilling the bark of Betula lenta, the Sweet Birch, or Black Birch, or Cherry Birch, or Mountain Mahogany of the Middle and Northern States and Canada. He also shows that only a very small proportion of the oil of birch, obtainable by the distillation, pre-exists in the bark, but that the oil is generated by the water and heat from two neutral substances of the bark, exactly in the same way that the volatile oil of bitter almonds is generated by a reaction between the emulsin and the amygdalin of the almonds.

Here, then, by this series of investigations made prior to 1845, it was shown that the volatile oils obtained by distilling with water the flowers of Spiræa ulmaria, the leaves of Gaultheria procumbens and the bark of Betula lenta, are identical in properties, reactions and composition, and that the chief element is methyl salicylate, and that these oils, so far as this element is concerned, are capable of being produced artificially from salicylic acid and methyl. When to this is added the knowledge that the destructive distillation of coal yields the carbolic acid, or phenol from coal-tar, and that this carbolic acid with sodium by Kolbé's process yields salicylic acid, and that the destructive distillation of wood yields methyl, the history and identity of these oils from various sources becomes fairly complete.

It will now be understood that the element of value in the oils is methyl salicylate, and therefore that the comparative value of the oils will be proportinate to the methyl salicylate each may contain. The oil of Meadow Sweet has never been an article of commerce, and no account of its proportion of methyl salicylate has been met with. Oil of wintergreen is said to consist of 90 per cent. of methyl salicylate and 10 per cent. of a hydrocarbon similar to terebene. This statement is upon the excellent authority of Prof. Procter.

Oil of birch is said by Pettigrew to be pure methyl salicylate, but this can hardly be true of the oil accessible in the markets, since several authorities state that in distilling the oil the distillation begins many degrees below the permanent boiling point. The oil may contain slightly more methyl salicylate than oil of wintergreen, and the proportion may be about 94 per cent. as given by some writers, but it is more probable that the oils are practically alike.

The artificial methyl salicylate is an oil hardly distinguishable from the others, and is probably, as ordinarily met with, of about the same degree of purity. Thus it would seem to make no difference which of these three was used as a therapeutic agent, except that for the present the artificial oil is much dearer without being any better, and it is therefore practically unused in medicine.

It is not surprising that three substances, though from such widely different sources, should be alike in sensible properties, when they are alike in chemical constitution, yet it would not be strictly accurate to say that in sensible properties they are indistinguishable. In samples selected as carefully as possible from this market the writer could detect but little difference in the odor even when the vapor was diluted by distance from the source of emanation and carefully and slowly inspired. Yet a trained expert in volatile oils did detect a considerable difference and told from the corks of the vials only, which was wintergreen.*

From the private history of the distillation of these oils for the market at the present time, however, it is very doubtful whether a specimen of true oil of wintergreen can be found. The wintergreen grows in the same localities as the birch, but according to the information obtained by Mr. George W. Kennedy, in a visit to a large distiller in Schuylkill county, Pa., the cost of collecting the birch for distillation is about $4 per ton, while the cost of collecting wintergreen is about $30 per ton. The yield of oil from the birch is about 5 pounds per ton or 0.23 p. c., and from wintergreen about 18 pounds per ton or 0.80 p. c., thus making the cost of the oil from wintergreen a little more than double that from birch, while the management of the supply of birch is much easier. Mr. Kennedy's very interesting paper describing this visit may be found in the American Journal of Pharmacy, vol. LIV., or Fourth Series, vol. XII., p. 49, February, 1882.

Other sources of unpublished information equally trustworthy represent the industry as carried on in other localities, as being extremely primitive and crude. Families of parents and children go into the woods for the distilling season; both sexes in trousers and all huddled under one rude shed with the stills at night, and all, excepting one, out collecting materials all day and the rude stills kept going night and day, supplied with all the wintergreen that may come handy, or be collected by the smaller children, while the larger cut down and chop up the much more plentiful birches. Thus all the history obtainable tends to the conclusion that almost all the oil accessible in the markets is distilled from varying mixtures of birch and wintergreen, the birch being always in much the largest proportion,—and that any oil which comes from either source alone is most likely to be from birch. From all the reading and inquiry possible to the writer it seems highly probable that no oil distilled exclusively from wintergreen is obtainable in the general market here, but that all is made from mixtures of birch and wintergreen in which the latter is present only in small proportion,—or from birch exclusively. Yet all this oil comes to market as oil of wintergreen, and is bought and sold almost entirely by this erroneous name.

In first hands it is generally, if not universally, known that it is oil of birch which they buy and sell as oil of wintergreen, but there is but little demand for oil of birch, while the demand for oil of wintergreen is large and constant, and almost all of it used for flavoring syrups, powders, soaps, etc. Under these circumstances it seems quite time that the small quantities used in medicine should be called by the more correct name of oil of birch, if only for the purpose of reducing the number of known substitutions. The U. S. Pharmacopœia should at least be free from this error, but it is not, and therefore lends its authority to perpetuate it. Physicians, who are willing to aid in correcting this bad usage by prescribing it as oil of birch rather than as oil of wintergreen, should write "oil of birch or the so-called oil of wintergreen," as there are many pharmacists, as well as physicians, who do not know the true condition of the markets in regard to this substance.

The oil is rather a costly substance, say $3.50 per pound, and being in large demand it is liable to adulteration. Being the heaviest of all the oils, the specific gravity is the best single test of purity. It should have a s.g. of 1.173. The chief adulterants are chloroform and oil of sassafrass, and these can be so used together as not to vary from the proper s.g., but they are easily detected by the Pharmacopœia tests.

The dose of oil of birch, like so many other therapeutic agents, varies much in different individuals, and no one can be sure that it has accomplished all that it is capable of doing until it is pushed to its physiological effect upon the individual under treatment by it. Like other salicylates it is rapidly eliminated, and therefore should be given from four to six times in the 24 hours in proportion to the severity of the case. Given in sufficient quantities in this way it will in 24 to 48 hours cause a ringing in the ears, and this is the physiological effect to be sought, and when found, a slight reduction of dose from that which caused the ringing will be the proper effective quantity.

Doses of ten minims four or six times a day will produce the ringing in some individuals, but if not it should be increased by two minims in each dose until the ringing is obtained. In this way doses of 16 minims will rarely have to be exceeded. Then a reduction of two minims will give the regular dosage to be observed.

It seems superfluous to say that the doses should be measured with accuracy and given with regularity, because it is so well known that active medicinal agents should always be so managed, yet it is a standing reproach to the profession that there is much hurtful inaccuracy in this respect. Much of the usage of this oil that is recorded has been by dropping, and without having the vials from which this dropping was done it is impossible to know what doses were really given. A four ounce prescription vial, taken at random, gave 185 drops to 120 minims of the oil. A two ounce vial half filled, with an average lip gave 197 drops to the 120 minims. Another similar vial which happened to have a thinner lip gave 216 drops to the 120 minims of oil, showing a range of error of over 30 drops in a measure of two fluidrachms.

An ordinary 12 minim dose would therefore be from one of these vials 18.48 drops. From another 19.68 drops, and from the third 21.60 drops,—a difference of over 3 drops in the dose, and if the doses were given 6 times in the 24 hours the difference per day would be nearly 19 drops, depending solely upon the vial used.

The use of a minim pipette avoids this irregularity. It is a convenient and inexpensive instrument, and is sufficiently accurate for all ordinary dosage.

There are two good ways of administering oil of birch. One is to deliver the dose into a four ounce vial containing about two fluidounces of cold water, shake the mixture actively, and then pour it into a glass and swallow it while in suspension in the water. The other way is to deliver the dose upon half a teaspoonful of powdered sugar in a glass, add about two fluidounces of water, stir actively and swallow at once while the oil is in suspension. The dose is not a very disagreeable one, and does not seem to cause disgust nor anorexia by frequent repetition.

In cases in which cod-liver oil is also indicated, it is very good practice to give them together. The strong flavor of the oil of birch entirely covers the fishy odor and taste of the cod-liver oil, and the latter oil agreeably dilutes the birch. Ten or twelve minims in half a fluidounce of cod-liver oil, swallowed after a mouthful of ice water will offend very few palates or stomachs.

Under the inspiration of mercantile profits, there is just now a good deal of drumming and advertising, throughout the country, of what is called by the advertisers and salesmen "true Salicylic Acid from Oil of Wintergreen," and the statements are so made as to contrast this with the artificial acid as being a deception, and it is most remarkable how many physicians are captured and held in captivity by these catchpenny inspirations from the pocket. This scheme is a fair example of a skillful hiding of the true truth behind a little false truth, with the expectation that if ingeniously done it will pay well; and such expectation is rarely disappointed.

The oil of birch does not appear to be a proper alternate or substitute for salicylic acid, or sodium salicylate in severe cases of acute articular rheumatism, since it does not appear to relieve the pain nor reduce the temperature as promptly; and this might be expected from the circumstance that when pushed to its physiological effects, it disturbs the hearing and sight less promptly and in an inferior degree. It seems to be most appropriately used in the milder attacks of gouty rheumatism or rheumatic gout which are so much more numerous, and which so often are the cause of protracted suffering and disability. These cases occur in hundreds, and the physician who can relieve an hundred of such is of more use to the community than one who makes a successful laparotomy, and more rapidly gets a better reputation; and beside he does more,—much more, in combatting quackery and pretense.

Perhaps the writer cannot better close this paper than by giving a typical case in which oil of birch was successfully used.

A married woman, aged 33, above the average height, weighing 160 pounds,—in vigorous health, and in active occupation, began to be disabled about the first of the year by a stiffness and discomfort, hardly amounting to pain, in both heels, felt at rising in the morning on some days and nearly absent on others, but wearing off during the exercises of the mornings. This gradually increased, becoming first slightly and then more painful on motion, causing an obstruction to walking, and to household occupations, and wearing off later in the day, not painful when at rest nor during the night, and no great inconvenience during the latter part of the day and the evening. In about two weeks this grew to be severe enough to call for advice and treatment. The tendo Achillis, and the heel about its insertion, were the seats of pain and disability. There was some tenderness on pressure, but not enough to render boots uncomfortable, and there was slight swelling in the fossæ on each side of both tendons, but no redness.

The first treatment was a half diet, and a teaspoonful of sodium bicarbonate in a goblet of water three times a day. This, as is commonly the case, acted as an aperient, increased the urinary excretion and rendered the secretions alkaline, but did not relieve the stiffness and pain, as it so often does in temporary chronic rheumatism. It did not even prevent a steady increase of the discomfort, for, after being continued for two weeks, there were days when walking was almost impracticable. Then for two weeks more the half diet was emphasized, and lithium citrate in doses of five grains, three times a day, was substituted for the sodium salt, but without improvement. The dose of lithium citrate was then doubled for a week, but without apparent effect. In these five to six weeks the patient's weight was reduced about three pounds, but the pain and disability had slowly increased, and now affected the spine of the tibia on both limbs, as well as the heels, and the pain was more pronounced, and the tenderness and swelling were slightly greater than before, in both localities of both limbs.

In this condition, on February 21st, the oil of birch was resorted to, beginning with ten minims every four hours during the day, or forty minims a day.

This dose was rapidly increased until ringing of the ears was obtained by the end of the second day, and the pain and discomfort were somewhat relieved. The dose was then reduced from the maximum of fourteen minims to twelve, and again to ten, as the pains diminished, and then she continued this dose until March 15th, when the oil was discontiued. By the end of the first week the pain and discomfort on moving was nearly gone, and by the end of the second week only the stiffness remained, with occasional slight pain at rising on some mornings. By the end of the third week of the oil this condition continued, but in a diminishing degree, so that the oil was omitted. From March 15th to the present time, April 5th, there has been occasionally a little discomfort on some mornings, with occasional over-indulgence in diet as a suspected cause, but with a gradual wearing off of all disordered sensation. When the condition was at its worst, and the local pain acute, morphine oleate was applied a few times with prompt relief. But beside this nothing was done that has not been mentioned. The half diet was of course a prominent element of the treatment in a patient who so favored the gouty element in the case, and it was the aim to reduce her weight from five to ten pounds. But it was only reduced three pounds during the first six weeks. Throughout the three weeks' administration of the oil, and since its discontinuance at the practical termination of the case, it has been reduced three pounds more.

The total amount of oil of birch used in the case was just two fluidounces.

The discussion which followed the reading of this paper before the Kings County Medical Association brought out a very considerable experience in the use of this agent in the treatment of rheumatism of various degrees of gravity. And one member presented a synopsis of what had been published upon its use so far as could be found.

Every physician who had used it frequently, had found cases in which it was either powerless, or was not well borne by the stomach, and some of these cases were afterwards benefited by sodium salicylate or salicylic acid. But all the testimony elicited was favorable to the use of the oil, and this especially in the large class of cases wherein the attacks were not severe. In all such it seemed to have important advantages over the sodium salicylate. In severe cases wherein the pain was very severe and the elevation of temperature great, the conditions were controlled more promptly and more effectually by the sodium salt.

There was no dissent from the general conclusion reached that the oil, whether natural or artificial, or whether from wintergreen or birch, was an important agent for obtaining the best results of salicylates in a very large class of cases.

NOTE ON VERATRUM VIRIDE, OR AMERICAN HELLEBORE.

BY EDWARD R. SQUIBB, M. D.*

There is probably no agent of the materia medica which has a more equivocal therapeutic reputation with the best authorities than veratrum viride. The two authorities upon which the profession of this country most rely, and to which reference is most frequently made, are the United States and the National Dispensatories. No ordinary practitioner who has never used the agent, but who has thought of using it, can read the accounts given of its medical properties and uses without a feeling that perhaps, on the whole, he had better let it alone. That very careful and conservative author, Dr. Alfred Stille, after having written all he had to say of the agent under its three heads in the National Dispensatory, concludes at page 1546 of the third edition, 1884, as follows: "It may be remarked here, as was implied in the account given of green American hellebore itself, that while some of our native physicians exalt this medicine to the rank of a panacea, others condemn its use altogether as scientifically illogical and practically dangerous. Among the latter we desire to be reckoned."

While this conclusion is the only reasonable one to be reached from the accounts given, it is evidently not given from actual experience, and can hardly be considered as final while so many physicians who make their own experience continue, generation after generation, to use it. In other words, it has not been stamped out. It has not,—at least for a great many years,—excited the zeal or enthusiasm of individual physicians, nor the cupidity of collectors and manufacturers, and has never been epidemic through advertisements and certificates, yet the writer distributes several hundred pounds of its preparations every year to a very steady demand, and knows of others who distribute much more than he does. It does not appear to be used much in large cities, and pharmacists dispense it infrequently upon physicians' prescriptions. It appears to go chiefly to country physicians, and those of the smaller towns, who dispense their own medicines; and when it is remembered that a large proportion of these are close observers, who make their own experience, and who know well what they can do with the comparatively few agents they employ, it is difficult to understand why they should so long continue to use an agent which is without advertisements and drummers, and has excellent authorities, with their trains of distressing effects, discouraging its use.

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* Read before The Kings County Medical Association at the stated meeting of June 7th, 1887.

But when the recorded testimony in regard to it is closely scrutinized, and as far as is practicable, freed from bias and confusion, there are important characteristics and individualities which must be admitted.

It is certainly a very potent and fairly manageable arterial sedative, much like aconite, but with a peculiar advantage over aconite in the degree to which, and the promptitude with which it reduces the force and frequency of the heart's action.

That is to say, there is rational and credible testimony showing that, without the prostration of nausea, the pulse rate can be reduced at will to any desirable point, and be held there for any reasonable time,—the respiration and temperature corresponding to the rate,—without hurtful prostration; and this cannot be done to a like degree by aconite.

This characteristic effect, and what it may therapeutically accomplish, is well illustrated by one of the experiments of Prof. H. C. Wood with the alkaloids of American hellebore, in a paper to be cited presently. The carotid of a Scotch terrier dog was accidentally cut while under the influence of the alkaloid, and the bleeding ceased spontaneously after a moment or two. Farther on in the experiment Dr. Wood says, "An attempt was now made to kill the dog by cutting the femoral artery at Poupart's ligament. The bleeding, however, ceased spontaneously in a very little while, without seriously affecting the dog. The force of the circulation had been so greatly lowered by the alkaloid that there was spontaneous arrest of hemorrhage in both carotid and femoral artery, without dangerous loss of blood."

May not this explain the influence of the drug over puerperal eclampsia, especially in relation to the similar influence of blood-letting over the same condition.

Like aconite, veratrum viride appears to exert no direct effect upon the cerebral centres.

The same nausea, vomiting, depression and prostration are described as following upon full doses of both these agents; but a comparison of the two, when given in the way that aconite is now used, is not found in the literature of the subject. The experience of its utility when so used is, however, the probable basis of the persistent reputation with a class of physicians who know what they can do with it, but who rarely record their experience.

It does not appear to be a duplicate of aconite nor to be as generally useful. But as an alternate of greater promptitude and power over the circulation, it can scarcely be without an individual and independent therapeutic value.

More than twenty years ago it was taken to pieces or dissected by Mr. Charles Bullock, of Philadelphia (see Amer. Journ. of Pharm., Third Series, vol. XIII., for September, 1865, p. 321, and Proceedings of The Amer. Pharm. Asso., vol. XV., for 1869, p. 360), and the result of his investigation was the separation of two alkaloids and an active resin. The physiological actions of these substances were investigated by Prof. H. C. Wood, of Philadelphia, and the results were published in The Amer. Journ. of Med. Sciences, New Series, vol. LIX., for 1870, p. 36, in a paper entitled "A Contribution to the knowledge of the Physiological Action of the Alkaloids Viridia, Veratroidia, and Veratria of Commerce, and of the Resin of Veratrum Viride." No advantage appears to have been taken by the use of the separated alkaloids, though they differed materially in their action upon animals, and the net result seems to have been that they were complementary to each other, and corrective of each other as they existed in the root, and that therefore there was no advantage in separating them.

The root, so far as the writer knows, has been mainly collected in two limited districts, although the plant grows in the swamps throughout the United States and Canada. The principal collection districts seem to have been the States of North Carolina and New York, and the drug was known in the markets as southern and northern hellebore. Its principal use has always been in the form of a powder to destroy insects upon growing plants, and for this purpose the northern American hellebore was commonly preferred. Of late years, however, the American hellebore has been almost driven out of the markets of this country by the European variety or veratrum album, and this wholly on account of price. The latter is imported at about 4 cents per pound, while the former can hardly be collected and dried in this country for less than 6 cents.

For medicinal use, however, it is believed that the veratrum viride has always been used, and the northern always preferred. The "rhizome and rootlets" are officinal in the U. S. Pharmacopœia, and from this a Fluid Extract and a Tincture are directed to be made.

It is questionable whether the Pharmacopœia be not in error in admitting the rootlets with the rhizome. Every issue of the Pharmacopœia up to 1880 directed "the root" or "the rhizome," the rootlets being included for the first time in the issue of 1880. All the recorded investigations of Osgood, Mitchell, Richardson, Scattergood, Percy, Bullock and Wood seem to have been based on the rhizome, and the writer has found no recorded experience upon which the change of 1880, admitting the rootlets, is based. Hence the writer's practice has not been changed to accord with the recent Pharmacopœia, but has continued in the use of the rhizome only, and this has been collected at the proper season, sliced and dried for him during many years by Dr. Wm. Manlius Smith, of Syracuse, N. Y. Properly collected under the personal supervision of a good physician and botanist, it has been hardly well enough paid for at 65 cents per pound. What, then, must be the value of the common drug of the market, which is sold at 6 to 9 cents per pound, collected probably at any season when convenient to go for it, roughly split and dirty, with rootlets attached, and dried with little respect to its importance.

The officinal Fluid Extract and Tincture are both made with strong alcohol, and the first represents the drug in the proportion of about one minim to the grain, and the Tincture two minims to the grain. The surplussage of having these two preparations is very apparent, and as the Fluid Extract,—especially if made by repercolation, is much the best, the Tincture should have been dropped. The reason for its continuance in the presence of a fluid extract was probably that a proprietary tincture was, and still is in very common use under the name of Norwood's Tincture of Veratrum Viride. This tincture is generally described as being made in the proportion of eight ounces of the drug to the pint, and as being a saturated tincture. It is, therefore, of the same strength as the officinal Tincture, but it cannot be saturated, because the Fluid Extract is double the strength.

On examination Norwood's tincture appears to be made from the commercial drug, or rhizome and rootlets together.

It is much darker in color than either of the officinal preparations, when these are made from the rhizome only. On evaporation it yields about 6.54 p. c. of extract, while the officinal tincture yields only 4.83 p. c. The Fluid Extract yields 12.26 p. c., but the extract from the officinal preparations is of a very different character, as is the behavior when the three are added to water.

The dose is a very important consideration in the use of this agent, as by a careful adjustment of quantity and frequency the disagreeable effects are, in great measure, avoided. Although it is a very potent agent and capable, when unskillfully used, of producing a most distressing train of symptoms, and very profound prostration, yet it does not appear to be very dangerous to life. In desperate cases of puerperal eclampsia it has been used in this city in doses up to a fluidrachm of the Fluid Extract, and this with success. But it is probable that in such cases very little of it is absorbed, even if the dose be not ejected by vomiting, for there are conditions of stomach in desperate cases wherein, as the elder Meigs used to say, "You might as well put your medicines in a wet bladder and hang this on a nail."

Except in emergencies the commencing dose should be small and rather frequently repeated, or, in short, it should be used just as aconite is used. The 3, 4 or 6 doses for the twenty-four hours should be added to as many tea or tablespoonfuls of water, and each given at the prescribed times after careful stirring of the milky mixture.

The commencing dose of the Fluid Extract for ordinary uses in reducing the force and frequency of the circulation and respiration should be about two minims every three hours, to be increased to three minims at the third dose, if no effect is perceptible by that time. But where an active congestion or a commencing inflammation is to be met by quickly reducing the damaging effect of rapid and forcible heart action, double this dose every hour or two hours must be used, and the risk of nausea be taken. Then, when a reduction to fifty or sixty pulsations to the minute is reached, smaller doses and longer intervals are indicated, and are to be so adjusted as to just keep the desired pulse rate.

The Tincture being of half strength, will of course be required in double quantity.

Like many other potent agents this Fluid Extract is often measured out by the uncertain method of dropping, and then the dose will vary beyond a practical degree of accuracy, with the size and shape of the lip of the vial from which it is dropped, with the fulness of the vial, and with the rapidity or slowness of the dropping. From an average one-ounce prescription vial when about half full, and the drops delivered slowly, there will be about 112 to 116 drops to 60 minims, or nearly two drops to the minim. But from a pocket-case vial with narrow square lip there are often not more than ninety drops to the fluidrachm, or one and a half drops to the minim. Any physician who will not use a minim measure, should at least ascertain the size of drop given by his particular vials of the liquids they carry. There is no small detail in common therapeutic practice more important than a fair degree of known accuracy in the dosage of potent medicines.

The meeting of The Kings County Medical Association for the consideration of veratrum viride as a therapeutic agent was opened by a paper of Dr. J. D. Rushmore, of Brooklyn. This paper, which gives a very complete summing up of the subject to the present time, and a careful examination of much recent experience collected with great care and labor, will be published in Gaillard's Medical Journal for November, 1887, and will doubtless command the attention it so well deserves.* It was followed by the foregoing note of this writer, and then the subject was discussed for the remainder of the evening. This discussion brought out much individual experience with the agent, chiefly, though not entirely, with reference to its use in puerperal eclampsia. The weight of the testimony elicited showed pretty clearly that the agent had a very great and easily manageable power of reducing the rate and tension of the circulation to any desirable extent, and of maintaining this condition at will, and that this could be done with entire safety, and under good management, without the distressing nausea and prostration which so often follow its less skilful use. This is easily and well accomplished in a majority of cases, though not in all, and when it is accomplished, and the pulse rate as an indication of the circulation, is held at or below 65, the seizures do not recur.

Often it was given by the stomach, but more recent experience has shown that some of its uncertainties and failures were probably due to the uncertainty of its absorption from the stomach in the condition wherein its prompt effect is most needed. Hence many practitioners now use it, especially in grave cases, by the hypodermic method, and both the Fluid Extract and Tincture had been largely used in this way without inconvenience and with very prompt result upon the pulse rate, and moderate doses frequently repeated were generally recommended in moderate cases which were seen during the early stages. But in grave cases and in advanced stages full or large doses were necessary in order to secure a prompt and certain effect. Eight to ten minims of the officinal Fluid Extract, or double that dose of the Tincture every fifteen minutes at first, and then every half hour, were considered to be a moderate rate of administration which in many cases would within an hour reduce the pulse rate to about 60. And when this reduction was accomplished the least possible quantity which would maintain the reduction should be quickly ascertained if nausea and prostration were to be avoided. One or two moderate hypodermic doses show the impression or the failure to impress any individual case and thus give the best indications for repetition or increase in quantity.

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*Dr. Charles Jewett, of Brooklyn, who contributed largely to the importance of the evening's discussion, has also a paper on the subject, which will doubtless appear in some prominent journal.

OPIUM ASSAY.

This subject is resumed after an additional experience of more than five years,—see EPHEMERIS for January, 1882, pages 2 and 14,—for the purpose of inviting attention to a number of slight improvements in the details of the process;—to emphasize two or more important points of the original process as published;—and to notice some criticisms and improvements of the process that have from time to time been published by others, as the process became popular.

In the first place it seems needful to give emphasis to the important point made in the first publication of the process,—namely, that it neither aims nor professes to be a critically accurate chemical analysis, but is only a pharmaceutical process of approximate assay, whereby with a very moderate degree of skill and experience the morphine value of all ordinary commercial opiums may be determined to within about a quarter of one per cent. In parallel assays of the same opium by two different persons,—or by the same person, there may be an occasional difference of .3 to .4 p. c. in result, but as a rule the difference should not exceed .2 p. c. and is often less than .1 p.c. And these differences are due oftener to want of skill and accuracy in working than to the process.

The process has been criticised as yielding results that were too high. This criticism can only be justified by weighing substances as morphine which are not morphine, and it is feared that this may have been done through a fault in the original paper in regard to the lime-water testing of the results, in order to correct them by the subtraction of matters insoluble in lime-water. This is given in the paper without particular emphasis, and merely as a test for the presence or absence of narcotine, when, though narcotine can hardly ever be present, other matters equally insoluble with narcotine are very often thrown down with the morphine and must be filtered out, weighed and subtracted for a proper correction of the results.

Another point too lightly considered in the orignal paper is the hygroscopic nature of powdered opium when this is to be assayed. Ten grammes of powdered opium was weighed off from a well put up stock package, and was exposed in a tared capsule to a moist summer atmosphere during about 8 days, being carefully weighed at stated intervals.

In 1 hour's	exposure	it gained	1.10 p. c.
" 2 hours'	"	"	1.87 "
" 24 "	"	"	3.26 "

A sudden change of weather to a cool dry air for about 24 hours then took it back, so that

In 48 hours'	exposure	it gained	2.10 p. c.
" 72 "	"	"	2.47 "

It was then dried at 100°C. or 212°F. until it ceased to lose weight, when it had lost from the original weight 3.40 p. c. Again exposed,

In 12 hours'	re-exposure	it gained	1.47 p. c.
" 24 "	"	"	3.19 "
" 48 "	"	"	3.88 "
" 60 "	"	"	4.20 "
" 72 "	"	"	2.50 "

From this and other evidence it is concluded that good powdered opium in the commercial condition should not lose more than 3.5 to 4 p. c., and that the results of assays should be calculated upon this proportion of moisture, whether the powder contains less or more.

The writer's present method is as follows,—referring to the original paper at p. 14 for minor details, and for explanation of the different steps,—and for sizes of vessels, filters, etc., all of which are still regarded as being of great importance in adapting the process to popular inexpert use.

In sampling moist opium much care is needed to get a just proportion of the various lumps, and to sample one lump in five in the way previously described, is safer than one in ten. The mass of samples should not weigh less than 20, nor more than 40 grammes. This, when rolled into a ball and cut in two, gives 10 to 20 grammes for each part, each to be carefully weighed,—one for drying to determine the moisture,—the other for the assay.

When powdered opium is to be assayed exactly, 10 grammes is a convenient quantity to be taken for each determination.

The opium is digested and frequently shaken during about 12 hours with 10 times its weight of cold water, the solution being acidulated with one or two drops of dilute sulphuric acid, if not already acid to litmus paper. The whole is then poured upon a wetted, tared filter, and drained and percolated with water well distributed upon the edges of the filter, and the residue by slow dropping from a pipette, until the filtrate measures in cubic centimetres about 15 times the weight of the opium in grammes. This strong solution is set aside to be evaporated last. The residue is then carefully returned to the digesting bottle, without injuring the filter, by means of a small spatula, and is again vigorously shaken with 5 times the weight of the opium of fresh water. The whole is then returned to the filter and drained, and the filter and residue are then well washed with successive portions of fresh water delivered by slow dropping from a pipette until the second filtrate amounts to about 15 times the weight of the opium. After this second filtrate is off,—making about 30 times the weight of the opium in all,—the residue is finally percolated slowly to the extent of about 20 c.c. more into a separate vessel,—this to be used instead of water for rinsing out the beakers and capsule farther on in the process. This is called the third percolate. The residue and filter are then dried and weighed for the proportion of insoluble matters.

In pouring the solution and residue onto the filter care is taken that in draining, the residue is not thicker upon one side of the filter, for then the subsequent washing of the residue will be imperfect from passing in greater proportion through the thin side than through the thick. This will generally happen if attention be not given to it.

The second percolate is evaporated in a tared capsule on a water bath until reduced to about twice or three times the weight of the opium. The first percolate is then poured in, and the vessel which held it is rinsed in with a small portion of the third percolate. The evaporation is now continued until the solutions are concentrated to about the weight of the opium,—or to not less than the weight, because then the solution is too thick and dense to be conveniently managed; and not more than one and a half times the weight, because then the solution for precipitation will be unnecessarily large, and therefore hold too much of the precipitated morphine in solution,—a portion that is always lost to the assay. Opiums vary somewhat in the amount and kind of soluble matters they yield to water, and some will yield too dense a solution when evaporated to the weight of the opium, but none have been met with which need be left at over one and a half times the weight.

At the end of the evaporation the extract should be fluid enough to be rinsed round the capsule when cold. This rotary motion given to it is kept up during five or ten minutes, or until the rings of extract which have dried upon the capsule are all entirely dissolved off. This dissolving will be moderately prompt when the extract is not more dense than a thick syrup. When but just thin enough to move round slowly the solution of the dried extract on the dish is less prompt, but still, with a little patience the solution will be complete.

The dense solution is then poured into a tared flask of the capacity of ten times the weight of the opium, and the capsule is rinsed into the flask with successive portions of 1 or 2 c.c. each of the third percolate, until the capsule is clean and the whole solution in the flask weighs not less than 1.6 times the weight of the opium, nor more than 2.2 times the weight. To this solution half its weight of alcohol, s.g. .817 to .820, is added. This proportion gives a mixture in which the extractive matters are most soluble and the precipitated morphine least soluble,—or rather a mixture which has these advantages after having been shaken with ether, for the ether immediately takes out a portion of the alcohol. The solution of opium and the alcohol are well shaken together, and then ether of a s.g. of about .725 is added to 1.5 times the weight of the opium, and the whole well shaken together. These additions first of alcohol and then of ether are very conveniently made by weighing, but if 10 grammes of opium be the quantity in process the measure of ether required will be about 23 to 25 c.c.

After the shaking together, aqueous solution of ammonia of s.g. .960,—10 p.c. solution,—is added to the amount of .4 the weight of the opium,— or 4 c.c. to 10 grammes of opium, and the whole is vigorously shaken until the crystallization of the morphine occurs, and the flask is then set aside over night for completing the crystallization. This proportion of ammonia is in excess for poor opiums, and is deficient for those which are very rich, but it is sufficient for such as do not contain over 17 p. c. of morphine, and is not in hurtful excess for such as contain over 10 p. c. Below 10 p. c. the proportion appears to entail a loss of morphine by rendering it more soluble in the mother liquors from which it crystallizes. A proportion of .3 or .35 the weight of the opium is better for poor opiums.

After standing over night the crystals of morphine will be seen in a layer between the watery solution and the ether, while a film of nearly colorless precipitate covers the bottom of the flask. This is probably meconate of lime.

The upper ethereal stratum is then carefully poured off as closely as possible, and when seen to be free from crystals, is thrown away. The original quantity of fresh ether is poured in and gently rinsed round the flask, so as to avoid making an emulsion, and yet mix thoroughly with the remainder of the first ether. This is poured off closely and thrown away like the first, and another equal portion of ether is used in the same way. Supposing each of the three portions of ether to have measured 23 c.c., that poured off the first and second times will be about this same volume, but the third will be somewhat less,—thus showing that the ether has washed out from the solution a part of the alcohol added, and showing that only about .015 or less of the original or first ethereal stratum can be left in the flask with the solution; and such a proportion would hardly be of much moment if wholly evaporated from the filters.

A pair of counterbalanced filters arranged the one within the other, so that four thicknesses of the paper are upon each side, are placed in a funnel and well wetted with fresh ether. The solution and crystals are then immediately poured into the filters, the ethereal layer going first. This remainder of the ether washings goes first through the ether wetted filters, but the dark liquid soon follows as the filters are filled up, and when all the liquid and most of the crystals are poured in, the edges of the filters and surface of the heavy liquid are washed with 3 or 4 c.c. of fresh ether delivered in drops from a pipette. If then there be any ether seen on the surface of the dark liquid, the funnel is tilted until it runs off by overflowing the edges of the filters.

While the crystals in the filters are draining, those remaining in the flask are washed down from the sides with the smallest quantities of water successively applied, and are poured into the filters, leaving the flask clean. The filters and contents are then well washed with successive small quantities of water delivered in drops from a pipette until the washings come off only moderately colored, or until the total of the mother liquor, washings and ether stratum does not exceed the measure of four times the weight of the opium, —40 c.c. from 10 grammes of opium.

The filters are then taken from the funnel, flattened on the contents at the folds, and pressed gently between folds of bibulous paper, so that as little of the washings as possible may be dried in the crystals. The filters are then opened, placed one upon the other, and dried at 100°C. or 212°F. until they cease to lose weight. If when half dried the mass of crystals be broken up, the time of drying may be reduced to an hour or two. The weight is then carefully taken, using the empty filter in the weight scale to counterbalance the other.

The entire contents of the filter are then transferred to a mortar, and rubbed to a uniform fine powder.

About .1 gramme of this powder is agitated in a test tube with 10 c.c. of lime-water, and if the powder dissolves to a solution which is very nearly or quite transparent, and from which no weighable precipitate settles out in an hour, then the contents of the filter are accepted as being practically, all morphine, and the weight of the contents multiplied by 100, and divided by the weight of the opium taken for the assay gives the percentage of morphine, the formula being—as the original weight of the opium taken is to the contents of the filter, so is one hundred to the percentage of morphine.

If the lime-water does not dissolve practically all the powder, as it will not in a large proportion of the opiums, then .5 gramme of the powder is accurately weighed and put into the flask with 50 c.c. of lime-water. A gentle agitation, without shaking, for one or two minutes dissolves all the morphine present, if in fine powder, but it is necessary to see that all the heavy particles are disintegrated and the soluble portions dissolved, continuing the agitation until this is certainly accomplished. If the lime-water be shaken a persistent froth will be formed, which renders the subsequent filtration imperfect, and canses much delay.

A pair of small counterpoised filters are arranged in a funnel, and being well wetted with water, the lime-water mixture is poured into them. The residue on the filters having drained the flask is rinsed into the filters by 3 to 5 c.c. of water in small portions successively used The filters and contents are then well washed with 5 c.c. more of water delivered by dropping from a pipette. The filters are then flattened on the contents, placed between folds of bibulous paper, and finally are dried at 100°C. and weighed. Then, as the .5 gramme taken is to the dried residue insoluble in lime-water, so is the total precipitate of which the .5 gramme is a part to the total residue which the whole precipitate would have yielded. This total residue subtracted from the total precipitate gives the amount of morphine from the assay; and this multiplied by 100 and divided by the weight of the opium taken for assay, gives the percentage of morphine.

In a paper entitled "The Estimation of Morphine in Opium by J. Howard Wainwright, Ph. B.," published in the Journal of the American Chemical Society, vol. VII., p. 45, the author in using this process advises *boiling* water for the extraction. But this is not an improvement, because it dissolves much narcotine, meconate of lime and organic matters that are rejected by cold water, and thus overloads unnecessarily the final solution for precipitation, and yields more colored crystals. The reasons given for the use of hot water are, first, that a smaller quantity is needed, and second, that the solution filters much more readily, and the magma is much easier to wash; but as there is no difficulty either in the exhaustion or the washing these advantages do not counterbalance the disadvantages.

In The Amer. Chem. Journal, for October, 1886, at page 295, vol. VIII., No. 5, is an important paper on "Opium Analysis, by Charles M. Stillwell, A. M." This expert analyst in his paper converts the above rather rude pharmaceutical procedure of this writer into a critical chemical analysis, and those who are experts in chemical work should by all means get this paper and follow it,—the details being very fully given for every step of the improved process.

The chief improvements made in the writer's process by Mr. Stillwell consist, first in washing the precipitate thoroughly with solutions previously saturated with morphine, and therefore entailing no loss in washing, while leaving the precipitate much cleaner; and second, by correcting the weight of the precipitate by dissolving out the morphine with hot alcohol instead of lime-water, drying the undissolved residue, weighing it, and subtracting the weight for a final result.

In the Chemical News of London, for February 2d, 1877, page 47, is a very instructive paper "On the Determination of the Amount of Morphia present in Opium, by E. F. Teschemacher, F. C. S. & C." In this paper the author advocates the use of a "morphiated spirit," or alcohol containing 1 part of ammonia water, s.g. .88, in 20, saturated with morphine and holding .33 p. c. ; and a "morphiated water" or water saturated with morphine, and holding .04 p. c. These are the washings adopted by Mr. Stillwell, and by their free use he gets the precipitate very clean without loss, as did Mr. Teschemacher.

The question which still remains unsettled is, whether the loss of morphine by washing with a limited amount of water, as in the writer's procedure, which leaves some coloring matter, etc., in the precipitate, is not fairly though roughly counterbalanced by loss of coloring matter, etc., when saturated spirit and water are copiously used. In the assays of two of the writer's assistants, working side by side, on the same opium, the one using saturated washings and the other water, the difference in results, so far, have been so small as to fall well within the limits of other errors to which the process is liable;—that is within the .1 to .3 p. c. variation in results.

It has been said of this process that if in a total range of from 8 to 18 p. c. it cannot come closer than .3 p. c. it is hardly to be commended, and this is true, if any other as simple and as easy of application by the hundreds of practical pharmacists who most need it, can be devised that is more accurate. In comparing this process with that of the U. S. Pharmacopœia in practice the latter is found to be more simple and easier of application, but it is much more variable in results from slight variations in management, while under the most favorable conditions for its application its results are from .75 to 1.5 p. c. too low.

That the writer's process does not give results which are too high,—but rather too low, is shown by the circumstance that assayed cases of opium have, within the past 5 years, been occasionally made up separately into salts of morphine, and the yield has commonly exceeded the assay. Again, it is certain that the assay solution after the ammonia reaction must remain saturated at its final temperature with morphine that is not accounted for in the result.

This loss in the mother liquor has been considerably reduced of late years by the farther concentration of the evaporated solutions. In an experimental trial of this point, a series of 8 assays of the same opium were made under conditions entirely uniform throughout, excepting that the solutions for precipitation were made to weigh 1.4, 1.6, 1.8, 2, 2.2 and 2.5 times the weight of the opium. When a distinct small difference was shown in a greater yield from the more concentrated solutions, excepting that when farther concentrated than 1.4 times the weight, the results were confused and uncertain from causes not ascertained.

Mr. Stillwell advocates the use of boiling alcohol, instead of lime-water, to separate the morphine for the final result, and the writer adopted his recommendation and was entirely successful with it, but it proved less prompt and more troublesome than the lime-water, and therefore a series of comparative experiments were made to determine which was the better solvent to use.

The series of eight parallel assays, previously mentioned, were managed in exact accordance with the detail given for the use of lime-water in separating the insoluble residue; and parallel with this use of the lime-water .5 gram. of each powder weighed off at the same time, was exhausted by alcohol, and the results obtained were as follows :

Residues by alcohol,	.0654	gram.	Residues by lime-water,	.0695	gram.
	.0612	"		.0638	"
	.0545	"		.0500	"
	.0485	"		.0587	"
	.0585	"		.0555	'
	.0518	"		.0583	"
	.0543	"		.0568	"
	.0526	"		.0535	"
Average,	.05585	"		.05763+	"

An accidental loss from two of the alcohol residues,—namely, the fourth and sixth, and from one lime-water residue,—the third, would require that these be omitted, and if omitted the averages became respectively,—by alcohol .05775 gram., and by lime-water .05873 gram. The progressive diminution in weight of the residues is due to the precipitation from solutions less and less concentrated as is noted above.

It was found early in the use of alcohol that the best way to manage it was to boil the .5 gram. of powder with a sufficient quantity of alcohol to hold all the morphine in solution when cold, and this quantity was about 75 c.c.; and the residue by alcohol being in very fine particles it was necessary to use good filters, and especially to avoid the creeping of unfiltered liquid over the edge of the inner filter into the outer one. It is quite possible that some of the discrepancies of the above given figures by alcohol are due to this creeping over into the outer filter, as they were watched by imperfect vision. The alcohol gives a nearly colorless residue, but a high colored solution, and if this latter be evaporated the morphine will crystallize very well, and provided the filter and residue have been well washed, the sum of the weights of these crystals and the residue will be not more than one or two millegrammes short of the original .5 gram. taken.

The use of lime-water requires no heating, and the 50 c.c. is sufficient to dissolve all the morphine with a fair degree of promptitude, and to hold it in solution indefinitely, and the residue being commonly flocculent has no tendency to creep over the edge of the filter. The residue by lime-water is much more colored than that by alcohol, and the filtrate less colored, and therefore the lime-water refuses more coloring matter than the alcohol, and this is probably the reason why the lime-water residues are heavier than those by alcohol.

The solubility of the dried residues was investigated as follows:— Both were rubbed to powder, and .01 gram. of the alcohol residue was added to 1 litre of lime-water,—1 in 100,000. On watching the powder as it slowly descended through the lime-water, the very finest particles seemed to disappear, but after frequent shaking during three days it was estimated that at least two-thirds of the coarser particles were dissolved. Another portion of .01 gram. of the powder was then added, and at the end of three days more of occasional shaking it was estimated to have disappeared in a less proportion than the first, so that about .01 gram. was supposed to be left undissolved, making an approximate or estimated solubility of the alcohol residue in lime-water of about 1 in 100,000.

The same amount of the lime-water residue was carefully dropped into a litre of alcohol s.g. .820, the same disappearance of the finer particles being noticed, but whether they really dissolved, or were too fine to be seen when disseminated through the liquid, is uncertain. At the end of a week, in warm weather, a very considerable proportion of the residue,—estimated at one-half,—remained undissolved.

The same quantity of alcohol residue was carefully dropped into a litre of the same alcohol, and was observed in the same way, but without any noticeable proportion of it being dissolved.

In consideration of these trials the writer much prefers the use of lime-water in the way now described in his re-written process, as being equally effective, while it is of much easier application.

ASSAY OF PERSIAN OPIUM.

Of late years Persian opium has improved so much in quality as to enter the markets in competition with the opium of Anatolia. Being now rarely absent from this market, and never absent from that of London, it occasionally comes up for assay. The process above given, though fairly applicable to it, is not so well adapted to it as to Turkey opium, chiefly because the Persian is so very different in structure and consistence, and so much more largely soluble in water. The Persian opium is in plano-convex loaves of fairly uniform size and consistence, each loaf being wrapped in paper, and often tied with a loose thread, and it is noticeable that the best quality met with thus far, had a wrapper of a rose red color. Inside the wrapper the surface is dry and smooth and without the poppy leaf wrapper universally met with in Anatolian opium. The very dry surface is very thin, and within this the structure of the loaves is very homogeneous and quite firm in consistence,—so firm as to cut almost like wax. The size and consistence of the loaves is so nearly uniform that the sampling of one loaf in ten, or one in twenty, is quite sufficient, and this is fortunate, because the cutting out of the cylindrical or conical pieces requires a strong knife and a strong hand, and is tiresome work. The consistence is such that when the cut is nearly completed the remaining part, not yet cut, often fractures with a snap and the cone flies out. An ordinary cheese sampler or tester sharpened, is very convenient for sampling opium,—especially for Persian opium. It cuts out a cylindrical portion of the lump, of any desired depth, and the sample is taken from the side of this cylinder by a knife.* The cut surfaces are not at all sticky, but on the contrary are rather greasy, and are polished by friction, and the circumstance that the opium does not adhere to nor soil the knife or the fingers, allows the sampling to be done with much greater accuracy than with Turkey opium, in regard to loss of moisture. The small pieces cut from the sides of the cones are put at once into a bottle or tin box, and are thus carried without loss of water until they are to be used for the assay. Then they are weighed carefully as they are. The weight being noted, and there being no tendency to stick to surfaces, the fragments are rolled together in the fingers, becoming softer by the warmth of the hand. The mass is then rolled out into a long cylinder and the two ends doubled into the centre, twisted, and again rolled out, and this repeated until a perfectly uniform mass is obtained, without the slightest loss of substance. The mass is then divided longitudinally into two or more portions,—one for determination of water and one or more for assay, and these are carefully weighed separately. When the weights of the separate portions are added together, the sum will be found to be much less than the original weight, and the loss of water by the manipulation is usually from 1 to 1.5 p.c., and this loss must be added to the weight of the portions weighed off to bring them to the original condition, as indicated by the first weighing of the total samples before manipulation.

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* A case of Persian opium recently carefully examined and assayed, weighed gross 194½ lbs. avoirdupois. It had a canvas cover which weighed 1½ lbs. The wooden case contained two cubical tin cases which held the loaves of opium packed in a chaffy, dusty, light, coarse substance. The wooden and tin cases, and packing powder weighed 39 lbs. The tins contained 207 of the plano-convex loaves of opium. Each loaf had an inner wrapper of thin, colorless rice paper, and an outer wrapper of much thicker paper,—white internally, and externally of a deep rose-red, and each was profusely wound round in all directions with thin, weak, loose thread. Both wrappers adhered to the opium so strongly that only a portion could be separated. The red paper, from its large amount of coloring matter of unknown composition, is very objectionable, and many ways to get it off were tried. The best way reached in these trials was to open out the duplicated folds on the flat side of the loaf and then immerse the whole, for a few seconds only, in cold water. Then with care the whole of the outer wrapper and a part of the inner one can be peeled off. The outer wrappers of the whole 207 loaves when dried, including the thread, weighed 2¼ lbs., and the inner wrappers,—estimated from the small parts

If the loss should be .3 gram. on an original weight of 30. gram. this would be 1 p. c. and would leave 29.7 gram. If this was divided into 3 parts for the assay, weighing say 10.2, 9.5 and 10. gram., then the formula for the calculation would be :

$$\begin{array}{lcccccccr}
\text{As } 29.7 & : & 30 & :: & 10.2 & : & 10.303 \\
\text{As } 29.7 & : & 30 & :: & 9.5 & : & 9.596 \\
\text{As } 29.7 & : & 30 & :: & 10.0 & : & 10.101 \\
\cline{5-5}\cline{7-7}
 & & & & 29.7 & & 30.000
\end{array}$$

and the resulting weights would be those upon which the results

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which could be detached, weighed ½ lb. Far the largest part of this inner rice paper cannot be separated, but must go with the opium into any process for working it

The gross weight being ....194½ lbs.
And the tare 1½+39+2¼+½ lb is.... .... 43¼ lbs.

Net weight, ...151¼ lbs.

The 207 loaves when air dried after the immersion and removal of wrappers, as far as practicable, weighed 151 lbs., giving a loss of ¼ lb.

The average weight of the loaves is therefore (151+207=) 11.67 ounces avoirdupois.

of the assay should be calculated. and not upon the weights as divided off after the manipulation.

The assay may be conducted by the process given for Turkey opium if great pains and care be taken,—especially in the application of the lime-water for correcting the obtained results of crude morphine.

In exhausting Persian opium with water the insoluble residue when dried does not weigh much more than half of that from Turkey opium, and consequently the evaporated solution is much more loaded with extractive matter, and from this ammonia throws down much that is not morphine. A very considerable proportion of this which is not morphine,—say eight or nine-tenths of it,—is however soluble in strong alcohol, and therefore alcohol cannot be used for this correction as proposed by Mr. Stillwell.

It is however rather better to modify the process of assay by a method of depurating the solution of opium devised and published by the writer in The Amer. Journ. of Pharmacy for March, 1860, p. 121.

In exhausting opium with water first, resinous substances are rejected. If this watery solution be evaporated to a small volume and the concentrated watery extract be then exhausted by strong alcohol, all the substances such as starch, gum, sugar, etc., are rejected and a depurated solution of the natural morphine salts in alcohol is obtained, and all substances insoluble in water and insoluble in alcohol are excluded.

In thus depurating the assay solution the process is modified as follows: The watery solutions of opium are evaporated as above described to about 1.25 times the weight of the opium, and the dense solution is then patiently rinsed round the large capsule until all the rings of extract are entirely redissolved in the solution. Then about 8 times the weight of the opium (100 c.c. for 10 grammes) of alcohol of a s. g. not above .820, is added to the dense solution little by little with constant stirring. The first additions of alcohol do not cause a permanent precipitate, and when the point of commencing precipitation is reached, all the extract is carefully dissolved off the sides of the capsule with the solution before more of the alcohol is added. Then the remainder of the alcohol is slowly added with active stirring, when the whole is closely covered and set aside for a few hours, or until the solution is perfectly clear. The clear solution is then poured off into a beaker, leaving the hard black residue adhering to the capsule. This residue is dissolved with 3 c.c. of water, and the sides of the capsule carefully washed down with this solution until the solution is complete and contains the whole of the residue. Then 25 c.c. more of alcohol are slowly and carefully stirred into this solution and it is thus again precipitated, and this time the mixture is boiled, and the loss of alcohol by boiling is resupplied, and the capsule, covered, is again allowed to stand until the solution is cold and quite clear. The clear solution is then added to the first clear solution in the beaker, and the solution and precipitation of the residue is repeated in exactly the same way. The accumulated alcoholic solution is then evaporated in a large capsule on a water bath,—without boiling, as there is always a loss by boiling,—to about the weight of the opium.*

At the end of the evaporation the extract should be fluid enough to be rinsed round the capsule when cold, and from this point the remainder of the assay process is carried out precisely as before described for Turkey opium.

The crude morphine thus obtained is much more easily washed, and is much whiter and purer than by the process as before described, and thus far in the writer's experience it is always so nearly soluble in both alcohol and lime-water that the weight admits of no correction. But, unless very carefully and skillfully managed it gives too low a result, or in other words does not account for all the morphine that is present in the opium, and the process itself is not so well adapted to general inexperienced usage.

In illustration of the difficulty there is in getting assays of opium to agree very closely, it may be mentioned that recently a lot of 8 cases or more of Persian opium was imported into this country from London, having been assayed in London by Mr. Teschemacher, whose paper on opium assay has been here quoted. The assay was 13.3 p.c. morphine, and the opium was sold as containing 13 p.c. of morphine. The buyer had it assayed by Mr. Stillwell, who has also been quoted here, and his assay made the opium 12.63 p.c. and 9 p.c. water. Upon this the buyer objected to the delivery as not up to the contract of 13 p.c. The seller insisted on his assay and disputed that of the buyer, and buyer and seller agreed to refer the question to this writer for a fresh assay.

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*A depurated solution of opium made exactly in this way has for more than twenty-five years been used by the writer as the basis for the Compound Solution of Opium (Liquor Opii: Compositus), and for the officinal Deodorized Tincture of Opium, and it yields preparations much less liable to disagree with persons sensitive to the disagreeable after-effects of opium.

The writer stated to the broker in charge of the transaction, that considering the difficulty in sampling Persian opium, the difference of only .67 p.c. might well be due to the sampling and not to the assay, and that the probability was that a third assay would not really help the matter, and that the question whether the assay was good or not might just as well be decided by lot or chance. But the broker directed the third assay to be made by the referee and it was carefully made. Four assays were made,—two by each of the processes here given, and two of the four turned out to be quite successful, with neither accident nor risk of loss, and these gave 12.965 and 13.102 p.c.—average 13.033 p.c., with 10.5 p.c. water and 23.24 p.c. of insoluble residue. Now while these results, from better opportunities for sampling, may possibly be some two or three-tenths of a per cent. more accurate than the preceding assays, they are only accidentally so, and any of the three assays might be, and should be accepted as about as close an approximation to the true value of the opium as the circumstances and conditions admit of,—and as practically sufficient.

Three individuals assaying a given powdered opium,—or the same sample of a moist opium should come within one or two-tenths of a per cent. of each other. But when assaying different samples of several cases of opium taken by different samplers at different times, it is not reasonable to expect them to agree more nearly than within six or seven-tenths of a per cent., and this instance fully warrants this conclusion, because two expert chemists of many years of well established experience and accuracy in such work, each working by processes which they have freely published and which are known to be good, could not differ as much as six to seven-tenths of a per cent., if working upon exactly the same substance, nor could be expected to differ less than that, when working upon different samples of a substance liable to variation.

During the last four years the writer has himself sampled and assayed 44 cases of opium in the moist condition,—22 cases of the commercial market grades, and 22 of the higher grades for his own use. Ten of the latter were of his own special importation for making powdered opium.

The 22 cases of commercial grades were in 5 lots, as follows:

8	cases,	ordinary,	minimum	9.2 p.c.,	maximum	9.5 p.c.	average	9.35 p.c.
5	"	"	"	9.0 "	"	10.9 "	"	9.86 "
2	"	selected, assayed together						11.65 "
2	"	"	"	"				10.90 "
10	"	"	"	"				11.56 "

The 22 cases of higher grade were all separately assayed, and comprised 12 lots of 1 to 3 cases in each lot.

14 cases of Salonica, minimum 13.1 p.c., maximum 13.9 p.c., average 13 65 p.c.
4 " " Yerli, " 12.3 " " 13.9 " " 13.14 "
4 " " Selected, " 13.8 " " 13.9 " " 13.85 "

These two groups happen to consist of 22 cases each, and give a total average of 10.66 p.c. for the one and 13.55 p.c. for the other group,—difference, 2.89 p.c. The difference in cost never exceeded 75 cents per pound, while the difference in morphine value was never less than 90 cents per pound, but was generally much greater, and therefore it was always better to buy the higher grade at the higher price by 15 cents per pound at the least,—and generally at more than double that economy; and this saving in buying the second group rather than the first would be at least $500.00, as the cases averaged over 150 pounds each.

When the opium is dried and powdered, the difference in value and the saving are still greater, and the reason why the lower grades are sold in the greater proportion of 50 cases to 1, is that the difference in appearance or sensible properties is slight even when the difference in real value is greatest. The remedy for this condition of the markets is to popularize and extend the application of all good processes of assay, and to give preference to those methods which are at the same time fairly accurate and best adapted to the largest number of hands with the least expert training and skill.

Early in the year reports were circulated in the opium markets that late frosts and droughts had so damaged the poppies, that the prospective opium crop would be short throughout Anatolia. Opium had been extremely low in price, and it was suspected that these reports might be the beginning of an upward speculative movement without very much basis. The area of opium production has been so extended of late years, that it is difficult to understand how either frosts or drought should be so general as to effect the entire crop, or any very large proportion of it. It is now pretty certain, however, that the crop will be very short,—probably not much over half of an ordinary crop, and therefore the advance in price has been very great and very steadily maintained, and the speculators have had the markets in their own hands. The new crop is now (July 25) beginning to reach Smyrna and Constantinople at fully double the prices of the latter part of 1886. A remarkable feature in this upward movement has been, that the prices in this market have been very much lower than in either Smyrna, Constantinople or London, and the difference has generally been as much as two shillings (English), or 50 cents per pound. This condition of market is difficult to account for on any other theory than that of a large stock on hand. This, if in the hands of many holders, produces a competition which keeps the price down. All the opium which is admitted into this country pays a duty of $1.00 per pound, and this must always be added to all foreign quotations in reaching the price here. It has not been very long since ordinary grades of commercial opium were sold here at about $3.00 per pound, and now these same grades command about $4.75. But if the same grades were now imported, they would cost here from $5.25 to $5.50, duty paid. This is the so-called "Druggists' Opium" of the foreign markets, and comes from districts whose names it bears, such as Karahissar, Balukesar, Kutajah, Ghevé, Eskishsir, and many more. The higher grade opiums are from Salonica, Boghaditch, Malatia, Yerli, Tokat and several more. But all these higher grades have what are known as "seconds,"—a quality not above the grades which constitute "Druggists' Opium," so that it does not do to buy by the district name. In the primary markets of Smyrna and Constantinople the district name goes far in regulating the price, and is commonly used in making quotations, and all opium is sold there either "tale quale" or "with visit." The first means that the buyer takes the opium as it may be, without the privilege of turning it out of the packages and inspecting it, and the other means that he may see the opium and inspect it as much as he pleases. All opium can be bought at a little lower price "tale quale," than "with visit." Beside these, there seems to be a grade of opium called "morphinerich," which the writer has had from the well-known house of Messrs. Ihmsen & Co., of Constantinople, to whom he is much indebted for constant information in regard to opium, scammony, etc. This "morphinerich" opium is selected from various sources by expert skill, and so far as yet tried it gives a very high assay,—quite equal to the Salonica variety.

POWDERED EXTRACTS.

There is a considerable pharmaceutical convenience in having extracts in the condition of powder, and whenever they can be powdered without overbalancing therapeutical disadvantages, they should be made in powder. This has for many years been the position of the writer, and upon it he has aimed to get as many as possible of the standard extracts into the condition of powder, even if the powder had to be a very coarse one. A very considerable proportion of the important extracts, however, have always resisted his efforts to dry them without material damage, and therefore they have had to be sent out in the pilular or moist condition. Although the pilular consistence is not a great inconvenience, and is no disadvantage to the well-trained pharmacist or physician, it has become very fashionable to require powdered extracts, and to refuse those which are not in that condition. And this demand has been met by many makers, so that now almost all the extracts are easily obtainable in the form of powder, though the strength of these powders is not always known.

Under these circumstances the writer has again gone over the subject recently, with care, and it may be worth while to record his failures.

Many extracts, when made with any menstruum that will ensure their therapeutic qualities, as representing the medicinal effects of the drugs from which they are made, cannot be dried so as to be powdered, at any temperature short of one that will either destroy or seriously damage them, and the only way that has ever occurred to the writer to get such extracts into the form of powder is by admixture with a sufficient quantity of some dry absorbent powder.

Take the important group of narcotic extracts for example, such as aconite, belladonna, digitalis, cannabis, conium, hyoscyamus, stramonium, etc., the active principles of which are all very sensitive to injury by heating. These even when evaporated to a pilular consistence are somewhat injured, and to powder them without farther injury an absorbent powder must be used, and this dilutes the extract, so that to a corresponding extent the advantages of the preceding concentration are lost. The class of Abstracts of the present revision of the U. S. P. consist simply of extracts thus diluted to the definite degree of representing the drugs in the proportion of one grain of abstract to two grains of the drug, and the probable reason why these have not come into use in the place of extracts is their feebleness. The physician reasonably finds that the use of one grain of an abstract instead of two grains of powdered drug, or two minims of fluid extract, is not a material advantage. So with powdered extracts, there must be some line or limit in strength or dilution, which should decide the usage for or against them. If abstracts are too feeble to come into use in place of extracts or as alternatives for them, this would go to show that a greater degree of concentration is required, and yet one of the most serious objections to the abstracts, is that they do not retain the condition of powder in warm weather, but shrink and are liable to become as inconvenient as extracts of pilular consistence. And farther dilution to reduce the risk of this would render them still more feeble.

It may probably be accepted that one grain of extract to two and a half of drug is about the lowest degree of concentration which would be acceptable in common usage, and the writer entirely failed to obtain this degree in many important extracts by the use of powdered sugar of milk as an absorbent and diluent. In some cases the powders could be made without exceeding this degree of dilution, and would remain in powder for days and even weeks, but sooner or later,—especially if the bottles were tested in a warm drying room at summer temperatures, the powders would shrink and become more or less hard. Frequently when the shrunken mass occupied not less than half the bottle, it could be broken up or scraped into a powder convenient enough for use, but not in a condition to be saleable without complaint.

Sugar of milk as an absorbent and diluent was then abandoned, and a sufficient quantity of the well-dried powdered drug was used, the mixture of powdered drug and extract being repowdered together after thorough drying. Such powdered extracts could be made considerably stronger than when sugar of milk was used; first, because less of such powder answered the purpose; and, second, because the powdered drug already contained its proportion of the extract. But such powders stood no better than when sugar of milk was used, or scarcely better.

Then the exhausted residue of the drug was tried. This can generally be made into a very fine light powder that is very absorbent, but it answered no better than the unexhausted powder, since the powdered extracts caked as badly as before.

These powders were tried as absorbents in various ways. First the extracts were made as dry as practicable, and the powders then stirred in, a gentle heat being continued till they almost ceased to lose weight. Next the powders were warmed and the concentrated liquid extract was added, with stirring, a little at a time, and a moderate heat continued until the mixture nearly ceased to lose weight. And finally the liquid was put upon the warmed powder, a little at a time, in the dilute form of a fluid extract, each addition being perfectly evaporated before the next addition, but all were practically failures.

Therefore, although the subject is not entirely given up, the conclusion is reached, that this writer cannot at present convert many of the extracts into a powder of one grain to two and a half of drug that will withstand summer temperatures without caking, and hence that it is therapeutically much better to dispense them of a pilular consistence, and give the approximate strength on the labels, and it has been found quite practicable to make this approximate strength fairly uniform. That is, to make it the same for different parcels of the same drug by being careful in the uniformity of the quality of the drug used.

Some extracts by careful management can be made into permanent powders, and all such should of course be so made, but how so many manufacturers get them all into the powdered condition the writer cannot understand.

CASCARA SAGRADA.

Rhamnus Purshiana is a sub-variety of the Buckthorn family of small trees and shrubs, which grow in most of the temperate climates. This sub-variety grows abundantly in California and Oregon, and the bark under the name of Chittem bark or cascara sagrada has been long known and used as a purgative, and the name cascara sagrada has more recently been usefully contracted to cascara. Some years ago it was taken up and pushed as a novelty, and by vigorous advertising, as a panacea for numerous ills, it has come into very common use, in the form of several pharmaceutical preparations.

There seems to be no doubt but that the bark of the branches, and a well-made fluid extract, and extract of this bark, are all effective simple aperients, not very disagreeable in taste or effect, easy of management, and not very liable to lose their effects by continuous use. And a prominent advantage in their use is that the dose may be adjusted in each individual case tò any degree of activity or mildness without leaving a persistent reaction.

These peculiar characteristics have long been known as belonging peculiarly to the bark of Rhamnus Frangula, and the use of this both in Europe and this country long antedated the use of cascara sagrada. And this longer and better known variety of the Buckthorn family was admitted to the present revision of the Pharmacopœia, because it was supposed to be the better medicinal agent of the two. Its supposed advantages over cascara are that while having all the advantages of cascara, it is milder, more pleasant and more manageable in effect and more agreeable in taste, and less liable to disturb stomachs and intestines which are sensitive or irritable. When properly used both are simple, mild, agreeable aperients, but the buckthorn the more simple and agreeable of the two, and required in somewhat larger quantities to give the same effect. Hence one or the other is superfluous in the materia medica, and it becomes important to know which should have the preference.

In order to assist in determining which is the better, large quantities of the two barks were carefully selected of uniform good quality, and from these exactly parallel extracts and fluid extracts were made, and have been placed in the hands of many close and careful observers, who are as little prejudiced as may be by the florid advertising, which one of the agents has received. By the parallel observations of many, made independently, it is hoped to obtain useful, if not conclusive, testimony.

Both barks are very plentiful and very cheap, and good qualities are easily obtainable of either at a cost of not more than 8 or 9 cents per pound by the bale. The buckthorn is much more uniform in quality than the cascara, and the inferior qualities of this, which are offered at 5 to 7 cents per pound, are better than the inferior qualities of cascara at similar prices. Both come long distances, and the freight on the buckthorn from Germany is less than upon cascara from California, and how it is possible to pay freights and two or three profits on them and sell them at such prices, is not easy to comprehend. The very different and inferior bark of the trunks and larger branches are rarely or never seen in buckthorn. But the markets are full of such bark from the cascara, and it is difficult to get even a few bales of the smaller quill bark which should alone be used. Both barks are said to improve very much in their medicinal qualities by age, and if so, it is reasonable to suppose that the preparations made from them also improve by age, but probably not so much as the barks do. Neither bark should be used until it is over a year old in the dry state, and this condition is more easily secured in the case of buckthorn than cascara.

The menstruum used for exhausting these barks by repercolation is important, and that which the writer has for many years used with buckthorn has been very successful. And there is hardly an instance known wherein the process of repercolation is more important or more successful. In another part of this pamphlet an example is given in detail of the management of buckthorn, and cascara was and is treated in exactly the same way with corresponding results, as far as the process is concerned.

This process gives preparations easily miscible with water, wine or syrup, and therefore easily taken and easily appropriated by the stomach and first passages.

HYDROCHLORATE OF COCAINE.

Since the last note on this subject, at page 906, nearly eleven months ago, this market has been well, though not abundantly, supplied with coca leaves at prices pretty steadily advancing, without any improvement in quality; and there has come to be two very distinct market grades, received chiefly by three or four different commercial houses.

The one kind is a light green, thin, small leaf so very much broken up, that hardly an unbroken leaf can be found. This contains a small proportion of stems and twigs, and quite a number of the yellow seed capsules. It has the appearance of having been beaten off of the trees, and certainly is not hand picked.

The other kind is a very much larger, thicker leaf, much less broken, of a duller, darker green, or brownish green color, and less uniform in color. A considerable proportion of the leaves are unbroken, and stems and twigs are absent or rare. This variety looks as though it was hand picked.

The first kind is called in the market Truxillo coca, and the lots now command as they arrive 23 to 25c. per pound. The second is called Huanuco coca, and about 30 to 32c. per pound is asked for it whether here or to arrive, an advance on both varieties of about 15 p.c. The localities which give the market names to these kinds are both in Peru, and considerably north of Lima,—the first near the coast, the other farther south and inland, but whether they come from these localities or not is uncertain, since names are sometimes used to conceal sources of supply. The present high price of Huanuco is based upon the customary report of a failure of a crop.

What has become of the fine quality of coca produced in Bolivia during the last six months is not known, none having reached either this market or Hamburg or London, so far as known to this writer. All received appears to have come from Peru.

The writer has used since his last report in these pages 238 bales of coca, 153 of the first variety and 85 of the second,—total, 41,858 pounds. The highest price paid was 32c and the lowest 15c., average 19c,—total cost, $7,957.00.

This was all manufactured into hydrochlorate of cocaine by the process given at p. 908* and gave a total yield as sold and in stock of 922,917 grains or 131 lbs. 13¼ ozs.

This was made and sold within the ten months following the last report, that is from November, 1886, to August, 1887, both inclusive, an average of about 13¼ lbs. per month, the demand pretty steadily increasing from about 6 lbs. per month to about 18 lbs.,—both the lowest and the highest being, however, exceptional.

All was sold in three forms, namely, as hydrochlorate, as 4 p.c. solution of hydrochlorate, and a small quantity as uncombined alkaloid.

A large proportion of it was put up with much labor and expense in vials of 5 to 30 grains each, and the loss in putting up, so as to give full weight in each vial, exceeds 6 p. c. The loss in putting up eighths, quarters, halves and ounces was about 5 p. c., and for larger quantities was insignificant. The available yield as put up and sold is therefore below the real yield by the amount of these losses, and of all other incidental and accidental losses, but it is what the manufacturer must always base all his calculations upon.

The available yield from 41,858 lbs. of coca being 922,917 grains, gives (922,917 ÷ 41,858 =) 22.05 grains of the salt to the pound of coca,—all being calculated as hydrochlorate.

As those who adversely criticise manufacturers' prices and profits generally do so without a knowledge of how these are made, it may be useful to give the details of this 10 months' experience, and in order to do this, a practically accurate account has been kept without attempting an approximation so close as to be complicated or confusing in detail.

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*In the last note on this process here referred to, the writer inadvertently omitted to mention an important improvement that had then been made in the process. Before the final solution in ether all the alkaloid is crystallized from warm benzene.

The entire 238 bales of 41,858 lbs., costing $7,957.00, was manufactured within 10 months, at the closely approximate cost, as follows:

Estimated rent of the necessary room for 10 months....	$34 00
Fixtures and apparatus of plant cost about $4,500.00.	
Interest and wear and tear on $4,500.00, 6 p. c....	27 00
Fire insurance, 2 p. c.; taxes, 2½ p. c....	20 00
Steam for heating, and power for mill....	250 00
Supply of water and gas....	40 00
160 lbs. of ether, at 60c....	96 00
9,000 lbs. of sulphuric acid, at 1½c....	135 00
5,425 lbs. of sodium carbonate, at 1.8c....	97 00
560 gallons of kerosene and benzene, at 10c....	56 00
Vials, corks, labels, wrappers and boxes....	275 00
Time and labor of 3½ men....	1,780 00
" " 2 girls....	480 00
Foreman, forewoman and office expenses....	380 00
Interest on $2,000.00 of coca and cocaine carried continually in stock, 4 p.c....	80 00
Total cost of manufacture....	$3,750 00
" " coca....	7,957 00
	$11,707 00

Net available yield of product above the cost of the coca....	$5,219 84
Less the cost of manufacturing....	3,750 00
Net profit....	$1,469 84

Then as $11,707.00 : $1,469.84 : 100 : 12.56 p.c. profit.

But 12.6 p.c. is not an adequate manufacturer's profit, unless the volume of the business be much larger than this, because a manufacturer with knowledge and experience enough for such a process would not be well paid by $1,470.00 in 10 months. Even on double this scale the manufacture of cocaine alone could hardly be carried on.

The market prices so far as known have not varied very much since the last note until about the middle of August. Considerable quantities of the hydrochlorate have been imported and occasional sales of large quantities in bulk have been heard of as low as $5.00 per ounce. How a fair quality could be sold at such a price after paying an import duty of 25 p.c., is not easy to comprehend. Makers here could not get a fair profit on it at less than about $5.50 in bulk in large quantities, or $6.00 to $7.00 if put up in small vials, vials included. But with the much higher prices at which coca has sold for some time past, the prices of the product have had to be advanced by about $1.00 per ounce, or about 15 p. c. to meet the similar advance on coca.

The character and quality of the product of the different makers have not changed materially within the past 10 months, but what change there has been is for the better only in appearance. Manufacturers have learned long ago the value of appearance in such products, and often the competition is for appearance rather than for intrinsic value. A large proportion of the buyers of cocaine salt, as of other chemical products, consider price first and appearance next, when neither may indicate high quality. But low price and fine appearance together always command the general market. The cocaine salt of only two of the five makers, the writer's product not being one of the two,—has a very white and very fine appearance, while all are probably nearly equal in true medicinal value, except from the presence of water in one.

The observations of the writer upon the reactions of the salt with chloroform have been continued and extended. Chloroform is a much better solvent of the salt as its s.g. is lower, —that is, as it contains more alcohol and water, and from this it follows, that the salt is more soluble in proportion to the water or alcohol it contains, whether the water be combined or accidental. Chloroform of good quality, such as the Purified Chloroform of the U. S. Pharmacopœia, has a s.g. of about 1.490 at 15.6° C. or 60° F., or 1.4726 at 25° C. or 77° F., compared with water at 15.6° C. as unity, and such chloroform contains from .500 to .552 p.c. of alcohol and traces of water. If .4 gram. of a given dry salt be soluble in 5 c.c. of this chloroform, the same quantity of the same salt weighed after exposure to the air on a damp day, will require less chloroform to dissolve it. Some specimens of the commercial salt lose weight on exposure to the air, while others gain in weight. The first class is very soluble in chloroform, and the second much less so, but the individuals of this class become more soluble as they gain more in weight on exposure. Some gain but little in an ordinary atmosphere and then cease to gain, and their rate or degree of solubility is then permanent. Others under the same conditions gain more and continue to gain longer, and reach a condition of very great solubility. These differences are due to the presence of a very small proportion of decomposition products which are very hygroscopic; and the proportion of such products seems to increase with time, probably from the known effects of water in splitting the alkaloid.

Chloroform, which has been recently well shaken with an equal volume of concentrated sulphuric acid, and allowed to separate completely, is practically free from both alcohol and water. Of such chloroform about 30 p.c. more is required to dissolve any given specimen of dry salt; but salt containing moisture is soluble in the same proportion as with unwashed chloroform. To illustrate the peculiar relations of moisture to this reaction 10 grams. of dry salt was added to 170 c.c. of chloroform, and the whole shaken until the chloroform was saturated, a considerable portion of the salt remaining undissolved in a condition which gave a satiny appearance to the liquid and undissolved salt while in motion after shaking. One-tenth of a c.c. of water added to this rendered it perfectly transparent in an instant. Again, .4 gram. of commercial salt taken dry from the vial required 5 c.c. of chloroform to dissolve it. The same quantity of the same salt exposed for two hours to the atmosphere of a rainy day gained .006 gram. or 1.5 p.c. in weight, and was then easily soluble in 2 c.c of the same chloroform.

When shaken out of the chloroform by the addition of three times its volume of ether, s.g. .720 to .725, much of the impurity is left in the ether and chloroform, but either there is a farther splitting of the salt, or enough of the original decomposition products are precipitated with the salt, to make it again require 5 c.c. of chloroform for solution when dry, but only 2 or 2.5 c.c. after ceasing to gain weight on exposure to air.

When the salt is dissolved in the same way in the smallest quantity of methyl alcohol or ethyl alcohol of about 90 p.c. or of absolute ethyl alcohol, and shaken out with ether much of the impurity remains in solution, but the salt still retains its relations to chloroform and the other solvents and to moisture, and is not improved much even in appearance. A salt with any very considerable amount of impurity would doubtless be improved very much by being shaken out of either of the solvents mentioned, by ether, and such very impure salts must have been in the hands of Mr. John Williams when in a paper read before the late British Conference he proposed the absolute alcohol and ether reaction, as a means of purification within the reach of everybody, but it is less effectual than where good chloroform is used in the same way.

The conclusions from these extended observations with chloroform are first, that in using the chloroform test, the chloroform must be of a definite high specific gravity of 1.490, and next that the salt must be first tested in its original market condition, and if found to be very soluble in this condition it must be dried, noting the proportion of moisture lost, and be then submitted to the solubility test.

Original and recent parcels of the four makers who chiefly supply the markets of this country, were again examined by chloroform in the order mentioned at page 916 et seq. In appearance they have changed somewhat in the past ten months, but in this respect not one of them yet equals the cheaper foreign products. Of No. 1, the .4 gram. was nearly all soluble in about 3 c.c. of chloroform, but the remaining very small proportion was not soluble in any amount of chloroform up to 15 c.c., and was evidently an impurity which should not have been present. No. 2 required 7 c.c. of chloroform for solution giving a perfectly transparent and nearly colorless solution; and when it was shaken out with ether, the ether residue was less than 1.5 p.c.

No. 3 was in semi-transparent, moist, granular crystals. The .4 gram. was soluble in .9 c.c. of chloroform. When shaken out with ether, it gave a residue of about 2.2 p.c. When exposed upon a tared watch glass, it lost weight so rapidly that it could not be closely weighed. In 24 hours it had lost about 4.2 p.c. In 36 hours the loss was over 5 p.c., and in 48 hours it was 7 p.c. Dried for 2 hours at 82°C. or 180°F. it lost about 10 p.c. Then re-exposed for 2 hours the loss fell to 9.03 p.c. and afterward varied very little from this during 48 hours.

The .4 gram. of this completely effloresced salt required 6 c.c. of chloroform for its solution, and when shaken out with ether gave a residue of about 2.4 p.c.

No. 4 was soluble in about 5.5 c.c. of chloroform, but otherwise was unchanged since the previous examination.

At the last examination two makers offered the salt in two forms at different prices, but now only one of these makers appears to offer two kinds,—one labelled crystallized and the other granulated.

All four appear to be sold in large and increasing quantities, and all, excepting one, are still liberally advertised. Occasionally it is reported (not through the advertisements) that one make is preferred to the others, but the preference appears to be about as often given to one as to another, so that by the test of extensive and prolonged use, they seem to be very much alike, and as the prices have differed but little, the test of prolonged usage is the more significant of practical uniformity in quality, although the difference in appearance and sensible properties is considerable.

The writer still searches in vain for anything in the cocaine salt resulting from his process of manufacture which answers to the descriptions of amorphous salt or of hygrin; and notwithstanding all that has been written upon the subject, he can get no evidence from his investigation of the products of this market, of the existence of either the one or the other. The residues of his own process when exhausted by benzene may contain one or both, but no time has been found to examine them. All the salts of this market appear to contain a proportion of foreign matter rarely less than 1 p.c. or more than 2.5 p.c., but this is a sticky, odorless, neutral substance of a light brown color and bitter taste, not irritant, and yielding the cocaine impressions upon the tongue, probably, because not completely freed from the salt of cocaine.

As no reasonable amount of pains, care and expense can entirely free the salt from this substance, it is inferred that there is a continuous production of it by the chemical manipulation, at the expense of the alkaloid. The writer has often supposed he had found an amorphous salt of cocaine, but in every instance thus far, crop after crop of crystals were sooner or later obtained from it until a very little sticky matter was left. These trials have always been in accord with the investigations of Dr. Ralph Stockman, of Edinburgh (see Pharm. Journ. and Transactions for April 23d, 1887, page 861), excepting that instead of anything answering to the descriptions of hygrin, he has only obtained the above-mentioned sticky substance in very small proportion. It is not difficult at any time to get a portion of the salt into a varnish-like condition with a transparent pelicle upon the surface, which may continue in this condition for weeks and even months, but sooner or later, especially if the pelicle be broken, distinct well-formed crystals will form and slowly grow until the whole is a crystalline mass with an estimated amount of 1 to 3 p.c. of sticky matter, or enough to prevent the crystals from being rubbed to powder without drying by a gentle heat.

In thus failing to confirm the existence of an amorphous hydrochlorate of cocaine, and of hygrin as a distinct alkaloid, the writer by no means ventures to deny their existence, but rather defers to the testimony of so many able chemists who have found both. He merely wishes to record his testimony that from his own experience, up to this time, he has obtained no convincing evidence of the existence of either substance in the cocaine salts of the markets. The inference suggested by some of his critics that self-interest, as a manufacturer, makes it difficult to convince him of what would imply an inferiority of his process and product, may be just. All that he ventures to say against the implied charge, is that more than 200 pounds of the product have been sold at prices slightly above the market without a single solicited sale or a single line of direct or indirect advertising. This quantity has been used all over an extended country for all the uses to which the substance has been applied, in direct competition with the products of all the other makers, for the whole period of three years, with sales continually increasing and without complaints of either irritation or inferior activity in use.

The irritant nature of the impurities of much of the European cocaine salt has been insisted on by very high authority there, and by inference, rather than by trial or examination, has been charged against some of the salts made here. As this charge was not improbable, diligent inquiry has been made of users here, thus far without any distinct evidence to sustain the charge.

FLUID EXTRACTS BY REPERCOLATION.

The published attempts of the writer to improve the character and the processes for the medicinal extracts and fluid extracts, commenced with a paper in The Amer. Journ. of Pharmacy, for January, 1857, and the subject has occupied much of his time and attention throughout the whole of the past thirty years. The progress made and the experience gained and corrected in twenty years of this time was collated and summed up in a paper published in the Proceedings of the Amer. Pharm. Asso. for 1878, at page 708. In this paper an account was given of an experience of about twelve years with the writer's process of repercolation, which had been first described in a paper in the volume of the Proceedings for 1866, at page 81.

The paper of 1878 was twice reprinted in pamphlet form, and was widely distributed with the hope of attracting attention to this important subject. That much attention was given to the subject is shown by the circumstance that the supply of pamphlets was exhausted five or six years ago, and that inquiries for them continue to the present time; and this perhaps will warrant a re-publication of the paper here, especially if it be supplemented by the progress and the corrections which the experience of the ten years last past can supply.

The paper is reprinted here exactly as it was published in 1878, with only the addition of some foot notes, but to save a repetition of the table of details of menstrua, etc., at the end of the paper, that table has been extended and corrected so as to represent the present practice as based upon the total experience in these details. Following the reprint will be found some corrections of the conclusions reached in the paper, and a short account of repercolation as used by the writer at the present time.

This method of extraction is believed to have become very commonly used in this country. Many manufacturers of extracts and fluid extracts on a very large scale have advertised their products for many years as being made by repercolation; and finally the last revision of the Pharmacopœia authorizes its use for its Fluid Extracts.

Repercolation as a title for this process has often been criticised adversely during the past few years, and has been occasionally rejected in favor of the only other title proposed,—namely Fractional Percolation.

To percolate is literally to strain through, and the word and process refer primarily to the liquid strained and only secondarily to the substance or thing through or by which the straining is done. To re-percolate is therefore to strain through again,—once or more than once.

This is the basis upon which the title was adopted, and although the title is objectionable, because the process is not a straining or filtering process at all, but one for exhausting solids of their soluble portions. Yet this is done by running or percolating the solvent liquid through the solid. The objection therefore lies against the word percolation; but this word having been authorized by long established good usage, the prefix, which merely qualifies or extends both the word and the process, must be in itself unobjectionable.

The error in the criticisms which have been noticed, lies in reversing the order of the elements of the process. The construction of the word will not bear the assumption that the substance through which the straining is done, is the primary element, and the liquid to be strained through it, secondary. If this relation could be admitted, then, certainly, there is no repercolation, for the substance is not percolated again, but is thrown away, and a fresh portion is taken, and through this the liquid is again passed, or strained or percolated.

The only substitute which has been proposed is Fractional Percolation, but the objections being to the word percolation, this does not avoid them. Fractional as a prefix is entirely applicable to any single portion of the indefinite or continuous series of portions, but it entirely fails to connect these portions with each other, and this re-using of the fractions is the distinctive feature of the process through which a distinctive title is required.

It is therefore concluded that repercolation is least objectionable of any titles that can be suggested at present, and it is now supported by more than twenty years of usage without having led to any confusion of ideas in its application.

REPRINT.

As the time approaches for a revision of the U. S. Pharmacopœia those parts of it which require the most time and labor should be recognized, that due consideration may be given to them ; and there is certainly no department of the work where more time and labor is needed than upon the fluid extracts and extracts. Should the Committee of Final Revision fail to find and adopt the best plan of making this important class of preparations, the Pharmacopœia, instead of being the model and standard of the nation, will be surely disregarded and left behind by the practice and the results of the large manufacturer, and the evil of the present will be confirmed and fastened upon the future.

It will not do for the committee to disregard any plan because it is laborious, or troublesome, or expensive, or complicated, or because it is not adapted to the knowledge and capacity of the large majority of physicians and pharmacists. These, though very important, are still secondary considerations. The thing to be accomplished in the Pharmacopœia is to have practically perfect preparations in every respect. That is, preparations that are really what they profess to be. They should contain all the active and useful parts of the drug in their natural conditions and associations ;

should reject as far as practicable the inert and useless portions of the drug; and should bear the established relation to the drug, of minim for grain; or, weight for weight, if this can be accomplished without materially disturbing the established relation. To effect this object a general scheme, plan or process can be adopted, and then every drug must be studied carefully and laboriously.

The original process of Professor Procter accomplished the exhaustion of the drug insufficiently, but that difficulty can be easily remedied by carrying the percolation farther. But the concentration of the weaker percolate to obtain the established relation between the drug and the fluid extract presents difficulties which are probably insurmountable by that process. It is not simply by the heat and oxidation of the evaporation process that all the harm is done to that portion of the preparation, but the active principles are so dissociated and split up by the concentration that they are no longer in their natural condition, but form new relations and combinations, which change their solubilities and bring a new set of reactions into play, making the preparation something else than what it professes to be. The evidence of this is found in the fact that a resinous or oleaginous drug can be thoroughly exhausted by a menstruum which will permanently hold all its constituents in solution. But if such menstruum be evaporated off, the same menstruum will not dissolve and hold the extract again. Nor will any other menstruum ever again reconstruct the extract or restore it to its original condition. For example, a diluted alcohol will exhaust buchu and will hold the oil while in its natural relations with other constituents of the leaf, in the same kind of combination or emulsion that exists in the leaf before extraction, and in such a solution, though very dense, the oil does not change in odor much, if at all more rapidly than the leaf does. But if such a solution be evaporated until the oil is precipitated and shows itself as a fully formed oil, the same strength of alcohol will not redissolve it. Nor will any strength of alcohol redissolve the whole of the extract, or recombine its once separated elements into their natural condition. And moreover, the oil, when separated, changes its physical properties more rapidly than when in its natural conditions in the leaf, or than when separated with its natural associations unbroken. These circumstances constitute the chief objection to the original process, and to many of the original menstrua of Prof. Procter, and led the present writer to try to make improvements both in the process and the menstrua.

This effort at improvement by the writer was begun in a paper published in the Proceedings of the Amer. Pharm. Asso. for 1865, p. 201.* To diminish the proportion of alcohol in the menstrua, and to economize its use, were the principal objects of this paper, and it is cited here for reference in regard to the importance of the points there insisted upon, because these points have not attracted the attention they deserve.

The effort at improvement was continued in 1866 by a paper published in the Proceedings of that year, p. 81. In this paper the method by repercolation was first proposed and described as overcoming the principal objections to the previous methods.†

This method of repercolation has now been exclusively used by the writer for nearly twelve years in the production of many thousands of pounds of all the principal fluid extracts, and the object of this paper is to sum up this experience, and publish the modifications of the process, as they have been suggested and successfully applied during this prolonged experience, with a view of bringing the process more prominently into notice in order to be critically examined and tested. The general results of the application of repercolation, in the writer's hands, are, that no other process yet proposed accomplishes the main objects so well; and therefore that unless some new process can be devised that may attain the objects better and more accurately than this, it should be the process adopted for the Pharmacopœia.

Papers by the writer in 1867 upon the same subject, as applied to the cinchonas, may be found in the Amer. Journ. of Pharm. for July, August, and September, and in the Proceedings of the Amer. Pharm. Asso. for 1867, p. 391. All the principles involved in percolation and repercolation were fully discussed and illustrated in these several papers, but they seemed to attract little attention, and they are cited here to avoid recapitulation, since they cover nearly every point which the writer has now to bring forward. But the papers also contain many details which accumulating experience has improved and materially modified.

About 1870 a new form and arrangement of percolator was devised by the writer, and was put into practice so successfully that two years later in the Proceedings of the Amer. Pharm. Asso. for

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*This paper embraces the percolations of Colchicum seed and of Calisaya Bark, chiefly, and gives important details of physiological testing of different portions of the percolate from the Colchicum seed.

† This paper treats mainly of the percolation and repercolation of Buchu, this drug being used for illustrating the process of repercolation.

1872, p. 182, an account of it, with a cut, was given in detail. This contrivance has now been in use continuously for about 8 years, upon every scale from 4 ounces to about 400 pounds, and by pretty thoroughly carrying out the principles involved in percolation, it has contributed very largely to the success and uniformity of the process in the writer's hands. But the apparent complication of this device, and the details of repercolation, seem to have operated against any general understanding of the process, so that it has probably been generally condemned without sufficient trial; while the physical laws which govern the relations between liquids and solids in the direction of discriminative solubilities have been still too much overlooked, in favor of the earlier and more simple processes.

Whatever may be said of the older processes in regard to simplicity and facility of application, by which they are adapted to any capacity, and thus go into general use, it may also be said with great certainty that under the ordinary conditions of their general use, they do not accomplish their object to a reasonable extent, or as well as other processes now known; and that, although the resulting preparations are put forth in the Pharmacopœia as representing the drugs minim for grain, they do not really come near to this relation. The variations in the quality of the drugs used, and the variations in the moisture which they contain, are elements of so much uncertainty and want of uniformity in the liquid preparations made from them, that it becomes very important to reduce all other sources of variability to a minimum.

Repercolation, well applied, leaves little to be desired in making a liquid preparation that will fully represent the drug in almost any desired relation of strength; and if indifferently applied, the inaccuracies of one operation are so made up and controlled by those which follow that when the results of the different operations or percolations of the process are mixed together the general results must practically be good and uniform.

Indeed, so satisfactory has this process been in the writer's hands for the last 8 or 10 years, that the difficulties of making good fluid extracts have been entirely confined to the getting of good materials to make them from, and in controlling the hygrometric moisture in such materials when used. And in view of the satisfactory results, the inconveniences of the process and the disadvantage of having to carry a large stock of the weak percolate from each drug, seem now to be of very much less consequence than at first.

Upon finding out how much more serious these inherent objections to repercolation appeared to others than to himself, and how little credit the process obtained for its results in the way of counterbalancing these objections, the writer set himself to the task of trying to simplify the apparatus and the process to the utmost extent that could be done without sacrificing the principles upon which the success depends; so that by doing away with the machinery and apparent complication of a special percolator, and as many details as possible, the process might appear less objectionable beside the older methods, and thus induce pharmacists to learn it and try it long enough to become expert at it, and to be able to judge wisely in regard to its practicability and its appropriateness to pharmacopœial use.

These efforts at simplification are now to be set forth for whatever they may be worth, and they may be best introduced here by a model process.

For this model process it may be well here, again, to take the most difficult substance known to the fluid extract maker, namely, cinchona bark. This was one of the substances investigated in the papers of 1867 above referred to, and they may be usefully read as including some points of investigation omitted here, and especially in regard to testing the alkaloid value of different portions of the percolates.

The cinchona used in the model processes to be given is of exceptionally good quality, and therefore exceptionally difficult to exhaust. It is a yellow cinchona from the C. officinalis cultivated in Java, and contains about 9 per cent. of total alkaloids, of which about 7 per cent. is quinia. It is therefore more than three times the value of officinal yellow cinchona, and when such barks are used for making the fluid extract, this should be reduced to some standard of strength. That is, the Pharmacopœia should direct that its fluid extract should have a definite alkaloid strength. In these model processes, however, this cinchona is used as if it was of the ordinary quality.

As the preparation of this paper for publication was undertaken by the special request of the Committee of the Amer. Pharm. Asso. on the Pharmacopœia for use in connection with their work of finding out the best way of making fluid extracts, the details of the processes must be given with a minuteness that may seem useless and tedious. Beside, it is a prominent object of the writer to show how, in his judgment, every individual fluid extract must be studied before it is adopted by the Pharmacopœia, if the utility and character of the Pharmacopœia as a standard for the nation is to be restored to it. Who is to do this work, and who is to pay for the time, skill, and labor necessary to do it well, are problems for the future.

The first most important question is that of a proper menstruum. The present officinal menstruum having proved objectionable soon after the Pharmacopœia was issued, a menstruum was adopted by the writer containing 109 parts alcohol of sp. gr. .817, 16 parts water, and 41 parts glycerin. This menstruum has now been in successful use for many years and affords good exhaustion, and a fluid extract which weighs 7685 grains to the pint. This is almost exactly minim for grain and weight for weight. But as the drug never is quite exhausted even under the very best management, the measure never should have been made minim for grain if the drug was to be fairly and fully represented by the fluid extract. As a rule of actual practice, the drug will not often be exhausted within 5 or 10 per cent., and by the officinal management, will fall greatly below this. A more accurate proportion would have been 90 to 95 minims to each 100 grains of drug, or about 8000 grains of drug to make a pint of fluid extract, each minim of which should represent a grain of the drug. Even by repercolation some such excess is needed to make the therapeutic relation what it professes to be. Beside this objection of being too close in theoretical relation to be true in practical value, this menstruum has long been believed to be unnecessarily strong in alcohol, and containing too much glycerin. The glycerin in many cases has a secondary use in menstrua which is hardly less important than its primary use as a solvent. It has the property of wetting substances, and permeating them to the exclusion of air, to a much greater degree than water or alcohol, and, when mixed with water or alcohol, imparts this property to the mixture. When used at all, therefore, it must be used with both these functions in view, and one step beyond this is objectionable. After a preliminary set of percolations with this old menstruum to observe how it would work on the small scale of 4 troy ounces of powder to each percolation, a new menstruum was tried consisting of 2 parts stronger alcohol, 2 parts water, and 1 part glycerin, and a preliminary set of percolations upon the same scale of 4 troy ounces gave good results, but proved that the scale was so small as to need especial skill and care in order to attain the desired accuracy.

Another tentative trial was then made with this new menstruum on a scale of 8 avoirdupois ounces at each percolation, and this proved to be a much less troublesome scale. And for cinchona it is about as small a scale as can be worked to advantage. An avoirdupois pound would be better and easier still. The details of these trials need not be given, and it is sufficient to say that they indicated, and gave a part of the necessary experience needed for another careful trial, in which two very important points were still to be settled, namely, the proportion of menstruum and weak percolate that was best to moisten the powder, and the length of time that was best to macerate each portion, the trials having shown that great variation was produced by both these elements. It was at first believed that 4 parts of liquid was sufficient to moisten 8 parts of powder, and that 24 hours was long enough to macerate, and the first two percolations of the following series were made with these conditions. In the third percolation the liquid was increased to 5½ parts, and the maceration kept at 24 hours. In the fourth, the liquid was increased to 6 parts. In the fifth, it was kept at 6 parts, and the time of maceration was extended to 48 hours. In the sixth percolation it was increased to 7 parts, and the moistened powder, covered closely, was allowed to stand 8 hours to absorb the liquid more thoroughly. Then the powder was passed through a No. 8 sieve, packed pretty firmly, filled with weak percolate and then macerated for 48 hours, making a total maceration of 56 hours.

The first percolation of the series, made with fresh menstruum throughout, is of course a simple percolation, and was carried to practical exhaustion. And this practical exhaustion was doubtless to within 5 or 10 per cent. of absolute exhaustion of all matters soluble in the menstruum. The residue was quite tasteless for more than half way down the percolator, and then began to be very slightly bitter. This bitterness increased until at the bottom of the percolator it was quite distinctly bitter, after percolation under very favorable circumstances with nearly four times its weight of menstruum.

It is quite certain that the extract obtained from a drug by percolation is not uniform throughout the percolation in its medicinal value. If the menstruum be well adjusted as a solvent of the active principles of the drug it will dissolve and carry out the most soluble portions first and in largest proportion, so that although doubtless some of the useful part continues to be present in all parts of the percolate and its extract, yet the proportion must dimish much more rapidly than the proportion of extract. This point is well shown, so far as cinchona is concerned, in a table given by the writer in the Amer. Journ. of Pharmacy for 1867, p. 402, where each portion of percolate and its extract were assayed for the total alkaloids they contained. Hence, though the quantity of dry extract yielded by different portions of the percolate be not a measure of the medicinal value of the percolate, it is still the best guide that is easily accessible. Bearing in mind then that medicinal exhaustion by percolation is more rapid than absolute exhaustion, and that the dry extract which measures absolute exhaustion becomes poorer in medicinal efficacy and richer in inert extractive matter, and that this divergence in value is greatest near the end of the process, the quantity of dry extract yielded by each fraction of the percolate is adopted as the most convenient measure of the rate and the extent of the exhaustion.

The want of uniformity introduced into this series of percolations by the variation in the quantity of liquid used to moisten the several portions of the powder, and the variation in the time of maceration, diminishes the value of the series as illustrative of the best results of repercolation, and made it advisable to add a fifth and a sixth percolation to show the true character of the process when fairly established in actual practice; and thus these two percolations become by far the most valuable of the series as results of repercolation in actual practice, whilst the formula and process merely show how to begin to use repercolation.

The formula and process now to be given embrace the experience obtained in making the series which it represents, and is offered as a model by which other trials should be made by other hands, with other varieties of cinchona.

Take of

Yellow cinchona, in powder No. 50,		32 parts.	
Stronger alcohol,*	s. g. .819 at 15.6° C =60° F.,		
	or s. g. .811 at 25° C.=77° F.,	2 parts.	For a sufficient quantity of menstruum.
Glycerin,	s. g. 1.250 at 15.6° C.=60° F.,		
	or s. g. 1.244 at 25° C.=77° F.,	1 part.	
Water,		2 parts.	

Weigh the stronger alcohol, glycerin, and water in succession, in any convenient quantity at a time, into a tared bottle, and mix them thoroughly for a menstruum.

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* It is hoped that in the next revision of the Pharmacopœia the "Alcohol" (sp. gr. .835) may be dropped, and the simple name Alcohol be applied to a clean spirit, of about the same sp. gr. here given.

Moisten 8 parts of the cinchona with 8 parts of the menstruum, by thoroughly mixing them, and allow the mixture to stand 8 hours in a closely covered vessel. Then pass the moist powder through a No. 8 sieve, and pack it firmly in a percolator. Pour menstruum on top until the mass is filled with liquid and a stratum remains on top unabsorbed; cover the percolator closely and macerate for 48 hours. Then arrange the percolator for an automatic supply of menstruum, and start the percolation at such a rate as to give 1 part of percolate in about 4 hours. Reserve the first 6 parts of percolate and continue the percolation until the cinchona is exhausted, separating the percolate received after the reserved portion into fractions of about 8 parts each.

Moisten a second portion of 8 parts of the cinchona with 8 parts of the weak percolate,—the portion that was obtained next after the reserved percolate,—and allow the moist powder to stand for 8 hours in a vessel closely covered. Then pack it moderately in a percolator, and supply the percolator automatically with the remaining fractions of the weak percolate in the order in which they were received, and finally with fresh menstruum until the cinchona is exhausted. Percolate in the same manner and at the same rate as with the first portion of cinchona, and reserving 8 parts of the first percolate, separate the weaker percolate into fractions of about 8 parts each.

Percolate the third and fourth portions of 8 parts each of the cinchona in the same way as the second portion.

Finally mix the four reserved percolates together to make 30 parts of finished fluid extract; and having corked, labelled, and numbered the bottles containing the fractions of weak percolate, set them away until the process for cinchona is to be resumed.

When this fluid extract is to be again made, repeat the process as with the second portion, and reserve 8 parts of the first percolate as finished fluid extract from each 8 parts of cinchona from that time forward so long as the fractions of weak percolate are carried forward with which to commence each operation.

In applying this formula and process each part was taken as an avoirdupois ounce, and therefore each percolation was made with a half pound avoirdupois of the cinchona; and the menstruum was made in a tared bottle from time to time as required.

As before stated, the series was made to consist of 6 percolations, and therefore the last 2 are in addition to the 4 of the formula, as if the process had been twice resumed, and the results of these 2 are entitled to most attention as showing the true practical character of the process of repercolation. And every percolation which might follow these can be demonstrated mathematically to approach nearer and nearer to accurate results the farther the series is extended, since every successive percolation tends to correct the errors and improve the accuracy of those which have preceded it.

For the purposes of this paper as a model, and to construct the following table, the percolate from the first five percolations of this series was divided into much smaller fractions than is directed in the process, or needed in actual practice, leaving for a subsequent table the model for actual practice. The fractions of the first 5 were somewhere near 2 parts or 2 ounces each, = 56.7 grams. It was not easy to get them uniform in weight, and therefore this was not attempted. Each fraction was shaken up and accurately weighed. Then about 1 cubic centimeter was measured off into a tared shallow watch glass, and quickly weighed to avoid loss by evaporation. These weighed portions were then dried by steam heat until they ceased to lose weight and the residue carefully weighed. This gave the data for calculating the total residue which each fraction would give if the whole fraction had been evaporated. But a large proportion of this residue was glycerin, and it was sought to get at the extract only. So a cubic centimeter of the menstruum was weighed and evaporated in the same watch glass until it ceased to lose weight under the same conditions, and it was found that the residue weighed 16 per cent. of the weight of the menstruum. This was an unexpected result, for as the menstruum contained 20 per cent. of its weight of glycerin, it was to be expected that upon evaporation very nearly this proportion would remain on the watch glass. Therefore the trial was three times repeated, and the mean of the trials was within a very small fraction of 16 per cent., showing that about 4 per cent. of the glycerin went off with the alcohol and water. This gave the remaining element for closely approximating the extract in each fraction by the following formulas. As the weight of the cubic centimeter taken from each fraction of percolate is to the weight of the residue after evaporation, so is the weight of the entire fraction to the weight of the residue it would leave on evaporation. But had this fraction been menstruum instead of percolate, and been evaporated under the same conditions, it would have given 16 per cent. of its weight of glycerin as a residue. It was therefore assumed (though of course not correctly) that 16 per cent. of the entire fraction was glycerin. Then 16 per cent. of the weight of each fraction was taken and this amount was subtracted from the calculated residue of the fraction, and the remainder was assumed as dry extract of cinchona. Next, as these fractions were not uniform in weight, the assumed extract did not represent a uniform proportion and rate of exhaustion. To show this rate of exhaustion better, a second proportion was made to represent it by percentage. As the total weight of the fraction is to the weight of extract obtained from it, so is 100 to the percentage of extract it contained. For example: The first fraction of the table weighed 62.72 grams. One c.c. of this fraction weighed 1.062 grams. This, dried on a watch glass, gave a residue weighing .488 gram. Then, as 1.062 : .488 : : 62.72 : 28.82. But this 62.72 grams. is assumed to give 16 per cent. of its weight of glycerin which does not go off by evaporation or (as 100 : 16 : : 62.72 :) 10.04 grams glycerin : and 28.82 residue less 10.04 glycerin leaves 18.78 as the approximate dry extract contained in the fraction of 62.72 grams of percolate. Then if 62.72 percolate give 18.78 extract, 100 percolate would give 29.9 extract, equal the percentage of extract contained in the fraction of percolate.

The remaining column of the table gives the difference in specific gravity at similar temperatures, between the menstruum and the various fractions of the percolates, and this also illustrates the rate of exhaustion, but in a way much easier of application in practice than that of weighing the extract.

The packing of percolators will vary, even with the greatest care and skill that can be applied, and such variations can never be known without some such investigation and record as given in these tables.

Such variations are commonly the result of too tight packing, so that some portion of the mass is so compact as to make the progress of the liquid through it slower than through other parts, and thus by its slower exhaustion the extract from it is added to the weaker liquor from other parts all the way along through the percolation instead of at the beginning, as is well illustrated in the fourth and fifth percolations of the table, where the percolators were packed too tightly.

REPERCOLATION OF CINCHONA: MENSTRUUM—STRONGER ALCOHOL 2, WATER 2, GLYCERIN 1, SP. GR., .9728 AT 20°C.

Portions of Percolate of about 2 ozs.=56.7 grams each.	First Percolation.				Second Percolation.				Third Percolation.				Fourth Percolation.				Fifth Percolation.				Sixth Percolation.			
	Grams.		Percentage of Dry Extract.	Difference in Specific Gravity.	Grams.		Percentage of Dry Extract.	Difference in Specific Gravity.	Grams.		Percentage of Dry Extract.	Difference in Specific Gravity.	Grams.		Percentage of Dry Extract.	Difference in Specific Gravity.	Grams		Percentage of Dry Extract.	Difference in Specific Gravity.	Grams.		Percentage of Dry Extract.	Difference in Specific Gravity.
	Weight of Portions of Percolate.	Weight of Dry Extract.			Weight of Portions of Percolate.	Weight of Dry Extract.			Weight of Portions of Percolate.	Weight of Dry Extract.			Weight of Portions of Percolate.	Weight of Dry Extract.			Weight of Portions of Percolate.	Weight of Dry Extract.			Weight of Portions of Percolate.	Weight of Dry Extract.		
1st Portion.......	62.72	18.78	29.9	.1312	60.51	17.09	28.2	.1160	62.41	20.23	32.4	.1468	62.41	19.50	31.2	.1484	51.06	17.76	34.8	.1640	.....	......	....	.....
2d “	59.85	16.09	26.9	.1112	55.76	17.99	32.3	.1292	56.24	14.07	25.0	.1180	58.61	15.46	26.4	.1300	63.06	22.57	35.8	.1684	.....	......	....	.....
3d “	57.63	13.54	23.5	.0960	60.48	18.53	30.6	.1244	59.20	10.93	18.5	.0908	57.63	11.25	19.5	.1000	63.68	19.82	31.1	.1536	.....	......	....	.....
4th “	58.62	11.97	20.4	.0836	58.57	12.70	21.7	.0912	62.49	13.06	20.9	.0984	48.15	8.68	18.0	.0900	[illegible]1.55	14.16	27.5	.1324	228.32	63.85	28.0	.1560
5th “	78.30	14.59	18.6	.0708	57.68	6.69	11.6	.0612	56.30	8.74	15.5	.0716	60.52	10.42	17.0	.0824	64.46	14.50	22.5	.1080	.....	......	....	.....
6th “	57.88	6.83	11.8	.0388	56.84	5.97	10.5	.0494	56.51	7.10	12.6	.0548	58.17	8.18	14.1	.0696	61.12	16.47	26.9	.1344	134.52	28.77	21.4	.1244
7th “	50.74	4.80	9.5	.0220	51.82	5.46	10.5	.0512	59.92	6.85	11.4	.0564	52.28	6.77	12.9	.0612	54.74	10.08	18.3	.0944	.....	......	....	.....
8th “	64.06	4.71	7.4	.0132	51.45	2.96	5.8	.0328	59.53	5.62	9.4	.0440	55.70	6.97	12.5	.0596	61.09	8.71	14.3	.0748	114.19	18.38	16.1	.0812
9th “	70.27	5.50	7.8	.0092	50.89	2.39	4.7	.0276	68.68	7.39	10.8	.0368	54.24	5.99	11.0	.0516	58.79	7.27	12.4	.0636	.....	......	....	.....
10th “	65.00	1.35	2.1	.0072	47.08	4.29	9.1	.0416	60.33	5.36	8.9	.0344	61.91	6.81	11.0	.0494	59.54	5.87	9.9	.0632	120.30	21.79	18.1	.0808
11th “	57.97	.79	1.4	.0040	56.38	4.04	7.2	.0304	53.76	4.11	7.6	.0376	60.57	6.78	11.2	.0480	59.02	5.09	8.6	.0448	.....	......	....	.....
12th “	56.30	......	..	.0024	55.55	2.11	3.8	.0182	57.93	2.55	4.4	.0324	56.85	6.47	11.4	.0472	58.17	6.54	11.2	.0424	108.61	11.42	10.5	.0472
13th “	51.94	.79	1.5	.0024	52.48	1.51	2.9	.0156	92.00	2.72	3.0	.0252	61.17	7.02	11.4	.0428	57.92	5.41	10.1	.0400	.....	......	....	.....
14th “	......	......	...	......	56.60	1.78	3.1	.0176	61.34	2.72	4.4	.0236	62.35	5.88	9.4	.0394	63.48	6.46	10.2	.0356	122.68	12.53	10.2	.0420
15th “	......	......	....	....	56.43	1.22	2.2	.0148	58.42	2.18	3.7	.0200	58.67	3.78	6.4	.0376	63.34	5.44	8.6	.0324	.....	......	....	.....
16th “	......	...	....	......	53.50	1.10	2.0	.0168	53.45	1.76	3.3	.0230	56.17	4.14	7.4	.0360	57.92	4.35	7.5	.0284	117.56	5.51	4.7	.0260
17th “	......	.....	..	......	57.90	2.25	3.9	.0168	48.75	1.46	3.0	.0244	60.12	3.04	5.1	.0332	58.32	4.43	7.6	.0264	.....	......	....	.....
18th “	......	......	....	......	55.24	2.67	4.8	.0156	65.36	3.34	5.1	.0304	64.82	3.59	5.5	.0280	65.30	3.75	5.7	.0212	119.79	3.43	2.9	.0200
19th “	......	......	....	......	68.22	2.78	4.1	.0152	66.56	2.32	3.5	.0156	53.92	1.88	3.5	.0240	59.91	3.46	5.8	.0188	.....	......	....	.....
20th “	......	......	....	......	86.88	2.49	2.9	.0092	65.24	1.91	2.9	.0116	55.06	1.14	2.1	.0208	60.20	4.17	6.9	.0180	122.59	.62	.5	.0196
21st “	......	......	....	......	......	......	....	......	51.99	.56	1.1	.0096	79.45	2.49	3.1	.0176	61.95	3.03	4.9	.0172	.....	....	...	.....
22d “	......	......	....	......	......	......	....	......	54.91	.91	1.7	.0072	63.58	.75	1.2	.0162	71.65	3.36	4.7	.0148	102.30	.....	....	.0200
23d “	......	......	....	......	......	......	....	...	72.44	1.40	1.9	.0052	61.52	......	....	.0124	74.81	.45	.6	.0128	......	.....	....	....
24th “	......	......	....	......	......	......	....	......	70.40	1.30	1.8	.0076	63.58	......	....	.0108	59.07	......	....	.0132	......	.....	....	.....
25th “	......	......	....	......	......	......	....	......	46.49	.54	1.2	.0046	57.27	.99	1.7	.0104	......	....	....	.....	......	.....	....	.....
Total	791.28	99.74	....	.....	1150.26	116.02	..	....	1520.65	129.13	....	.....	1484.72	147.98	....	......	1455.54	193.15	....	......	1290.86	166.30	...	......
Reserved Extract..	......	48.41	....	......	....	66.31	....	......	....	58.29	....	......	....	54.89	....	......	....	74.81	....	......	....	63.85	....	......
Extract carried forward	......	51.33	....	......	....	49.71	....	......	....	70.84	....	......	....	93.09	....	......	....	118.34	...	......	....	102.45	..	......
Actual Extract obtained...........	......	99.74	....	......	....	64.69	....	......	....	79.42	....	......	....	77.14	....	......	....	100.06	....	......	....	47.46	....	......

In interpreting the results of this table the disturbing effect of the trials of different degrees of moistening and different length of maceration, must be borne in mind as largely concerned in the discordant results. But this discordance fairly shows first the necessity for careful investigations and trials, since otherwise the discords would have escaped observation; and next shows the certainty with which each operation tends to control and correct the results of the preceding one until uniformity be reached. The residues in the percolators were critically examined by tasting, and in none was the exhaustion absolute. As the percolators were emptied the upper eighth would be tasteless as a rule; then the bitter taste would be perceptible and would gradually increase to the bottom. At three-fourths down it would be very decided, and the remaining fourth would be pretty strongly bitter. The different percolations were only moderately uniform among themselves, and the want of uniformity was mainly in the lower third of the residue. But the residues were much more uniform among themselves than were the proportions of extract obtained, and all were fairly exhausted. The first and sixth percolations gave the most thoroughly exhausted residues, and yet the extract obtained, as shown by the table, was about two to one. This shows in a striking way that the extractive matter is not a measure of the exhaustion as judged by the bitterness of the residue. Therefore in using the quantity of extract as a guide to exhaustion, if the quality of the extract be not ascertained the condition of the residue must be used as a check upon the extract as a guide.

The general result, however, as shown by even a glance at the table—a result that could be obtained in no other way—though favorable to repercolation, is unexpectedly unfavorable to the menstruum used because of the overloading and masking effect of the excess of soluble extractive matter in this exceptionally rich, soft, soluble bark. Therefore another percolation—the seventh of this series—was made with another grade of cinchona, using the same weak percolates and menstruum. This cinchona was the poorest in the writer's possession. It is from the C. officinalis cultivated in Ceylon, and contains between 4 and 5 per cent. of total alkaloids, of which about three-fourths is quinia. Therefore though still much richer than the U. S. P. yellow cinchona it is much nearer to it than the Java cinchona is. This 8 ounces =226.7 grams of the new powder was as well exhausted as the other percolations with 1136.33 grams of percolate in 5 portions of about 8 ounces = 226.7 grams each. These portions, by the same calculations, yielded respectively 59.85, 37.26, 22.16, 7.15, and 2.77 grams = 129.19 grams of extract. Of this 102.45 grams was carried forward to it in weak percolates from the sixth percolation of the table. The 8 ounces = 226.7 grams reserved contained 59.85 grams of extract, leaving 4 portions of weak percolate to be carried forward containing (129.19 — 59.85 =) 69.34 grams of extract. But the extract which appears to have been obtained by this percolation is only (129.19 — 102.45 =) 26.74 grams, and yet the powder was about as well exhausted as any of the previous percolations, and the weak percolates carried forward were much less loaded with extractive.

This improvement of the process by the use of a less exceptional quality of cinchona was however still evidently insufficient, and left it still short of the best results. The menstruum was next to be changed, as it plainly needed more alcohol to exclude some of the extract, and probably less glycerin.

A new menstruum was made consisting of 5 parts stronger alcohol, 4 parts water, and 1 part glycerin. The sp. gr. of this mixture was .9575 at 15.6° C. = 60° F., or .9496 at 25° C. = 77° F. A cubic centimeter of this menstruum carefully weighed and evaporated on a watch glass left 7.75 per cent. of glycerin not evaporable at the temperature to which the fractions of percolate were submitted. A new series of percolations was started with this menstruum, and was conducted precisely as with the former series. The first two percolations were made with the rich Java cinchona so as to compare the results of the two menstrua upon the same powder. The remainder were made with the Ceylon powder and new menstruum. In this series the percolate was divided into portions of 8 ounces = 226.7 grams each except the first portion of the first percolation, which was 6 ounces = 170.1 grams, and the powder in each was moistened with 8 ounces = 226.7 grams of menstruum or weak percolate. So moistened it could not have been passed through the sieve at once, but by standing for the prescribed 8 hours in a closely covered vessel the liquid was absorbed by the powder, and then it was easily passed through the sieve. When moistened to this extent the powder must not be firmly packed, and it is quite important to use the largest practicable quantity of liquid to moisten the powder in repercolation. The results of these percolations are given in the following table.

REPERCOLATION OF CINCHONA.—MENSTRUUM, 5, 4, AND 1, SP. GR. .954 AT 20° C.=68° F.

8 Avoirdupois ounce=226.7 grams of Powder for each Percolation. Total Percolates in 4th, 5th, 6th, and 7th Percolations, each 1586.9 *grams.*

Portions of Percolate of about 8 ounces = 226.7 grams each. The 4th, 5th, 6th and 7th Percolations were made exactly 226.7 grams each.	JAVA CINCHONA.							
	First Percolation.				Second Percolation.			
	Grams.				Grams.			
	Weight of Portions of Percolate.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.	Weight of Portions of Percolates.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.
1st portion	170.20	48.44	28.4	.1264	226.93	74.77	32.9	.1384
2d "	226.80	31.42	13.9	.0672	227.00	45.31	20.0	.0880
3d "	226.75	8.02	3.1	.0102	226.85	5.95	2.7	.0180
4th "	206.17	2.96	1.4	.0052	226.78	3.88	1.8	.0092
5th "	114.61	.87	.3	.0060	226.83	2.60	1.1	.0124
6th "	......	.....	.....	.....	......	......	....	.....
7th "	......	.....	.....	.....	......	......	....	.....
Total	944.53	91.21	..	.....	1134.39	132.51	.....	.....
Reserved Ext.	......	48.44	....	.....	....	74.77	.....	....
Extrct. carried forward	......	42.77	.....	.....	....	......	.....	.....
Actual extract obtained	......	91.21	.....	.....	....	57.74 89.74		

Portions of Percolate of about 8 ounces = 226.7 grams each. The 4th, 5th, 6th and 7th Percolations were made exactly 226.7 grams each.	CEYLON CINCHONA.															
	Third Percolation.				Fourth Percolation.			Fifth Percolation.			Sixth Percolation.			Seventh Percolation.		
	Grams.															
	Weight of Portions of Percolate.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.	Weight of Dry Extract.	Percentage of Dry Extract.	Difference in Specific Gravity.
1st portion	226.84	58.18	25.7	.1048	71.05	31.3	.1428	73.67	32.5	.1516	73.85	32.6	.1636	73.03	32.2	.1598
2d "	227.11	28.00	12.3	.0480	47.43	20.9	.0936	52.71	23.3	.1076	52.90	23.3	.1184	50.14	22.1	.1080
3d "	226.80	17.94	7.9	.0340	25.16	11.1	.0688	23.02	10.2	.0460	20.96	9.2	.0520	26.38	11.7	.0590
4th "	227.00	15.35	6.8	.0268	20.60	9.1	.0232	9.60	4.2	.0208	8.04	3.5	.0184	11.11	4.9	.0210
5th "	226.91	8.84	3.9	.0192	6.80	3.0	.0100	7.31	3.2	.0092	8.70	3.8	.0036	10.38	4.5	.0208
6th "	226.70	2.33	1.0	.0140	5.26	2.3	.0036	2.62	1.2	.0008	1.40	.6	minus.	4.50	2.0	.0092
7th "	226.82	1.29	.5	.0090	1.14	.5	.0020	1.53	.7	.0006	.37	.2	minus.	.60	.3	minus.
Total	1588.18	131.93	.....	.....	177.44	......	......	170.46	......	......	166.22	......	....	176.14	....	....
Reserved Ext.	....	58.18	.....	.....	71.05	......	......	73.67	......	......	73.85	......	....	73.03	....	....
Extrct. carried forward	....	73.75	.....	.....	106.39	......	......	96.79	......	......	92.37	......	....	103.11	....	....
Actual extract obtained	....	74.19	.....	.....	103.69	......	......	64.07	......	......	69.43	......	....	83.77	....	....

This table fairly represents the application of the formula and process given at page 1002 in all the details, and the actual practice of repercolation, only that the results are imperfectly examined and recorded here, for illustration by means of the table; and the table is presented as a model upon which every individual fluid extract should be studied. The weighings and measurings are not chemically nor critically accurate, nor is the basis of calculations mathematically correct. And when differences of specific gravity are given to the fourth decimal place, the reader must not accept them or any of the figures as having anything like the extreme degree of precision which would be indicated by such figures. The weighings in all the tables were made to the nearest centigram, and the specific gravities were all taken in a rather rudely made 25-gram flask, without corrections for temperatures, and the four decimal places come from multiplying the weights obtained with this flask in centigrams by 4. Hence these differences of sp. gr. although put down with the apparent accuracy of four decimal places are really the least accurate of all the determinations of the tables. In short the whole results should be taken as being only close and useful approximations, and such as most pharmacists could easily make. This table being the last of all, and not half completed when the paper had to be sent to the Amer. Journ. of Pharmacy for publication, embraces the experience and skill acquired in making the others, and its better results are therefore partly due, no doubt, to the dexterity obtained by a few months of personal practice on this small scale of working. It therefore may be accepted as representing good ordinary practice with repercolation as applied to one of the most difficult substances known, on the lowest scale of quantity likely to be needed by the pharmacist, and the fluid extract yielded seems to be of unexceptionable quality in every respect, both in sensible properties and when applied therapeutically in two cases. It is unfortunate that the presence of glycerin not only prevents the precipitation of alkaloids by ammonia, but also entirely invalidates the thalleioquin test as applied to the percolates; and that no test was found whereby to judge of the quantity of alkaloids in the different percolates better than by mere taste and color. The final percolates were always very decidedly bitter, and never paler than a dark sherry color even when yielding not over one-tenth of one per cent. of total extract. Two very curious apparent results in the table are well worthy of farther and more accurate observation. First, that the quantity of extract obtained from the different percolations as measured by that of the first simple percolation with new menstruum is in the aggregate over 100 per cent., while the exhaustions are apparently not so good as the first. The other result, which leads in the same direction, is that the difference between the sp. gr. of the menstruum, and the sp. gr. of the weaker percolates diminishes more rapidly than it should do, and finally gets to be a minus quantity, which *a priori* should be impossible. All this leads to an inference that the residue left behind in the percolator splits up the menstruum, and holds on to more of the water or more of the glycerin, or more of both, than it does of the alcohol.

This table again illustrates the disturbing effects of insensible variations in the packing of percolators, and how by repercolation such variations are so controlled as to give fairly uniform results in practice.

It remains now to give a summary of the results obtained from these two series, as bearing upon the relation between the weight and measure of the reserved portion of each percolation.

FIRST SERIES OF PERCOLATIONS.				SECOND SERIES OF PERCOLATIONS.			
Reserved Portions.	Weight. Grams.	Measure. Cubic Cent.	Difference Per cent.	Reserved Portions	Weight Grams	Measure. Cubic Cent.	Difference. Per cent.
1st Percolation, ...	171.10	158	7.6	1st Percolation.....	170.20	158	7.1
2d "	226.80	214	6.0	2d " ,...	226.90	210	7.5
3d "	226.80	210	7.5	3d "	226.80	216	5.0
4th "	226.80	208	8.8	4th "	226 80	208	8.8
5th "	226.80	204	10.1	5th "	226.80	206	9.1
6th "	226.80	201	11.4	6th "	226.80	206	9.1
7th "	226.80	206	9.2	7th "	226.80	211	7.0

It will be seen by this table that the first series gives a relation varying between 89 and 94 minims to each 100 grains of the cinchona; and for the second series gives 90 to 95 minims to the 100 grains as the extreme limits of the series. Either of these is a great improvement upon the results of pharmacopœial practice.

The deductions which the writer draws from the work here given as applicable to the present pharmacopœial practice, and that which may be desired for the future are mainly as follows :

First. That the present formulas and processes for percolation are so defective that the relation to the drug which they profess is not practically accurate either as to quality or quantity, and therefore that a better process is greatly needed.

Second. That the process by repercolation, though it has some grave disadvantages, and is liable to defects in practice, yet gives far better results, both in quality and quantity of product; while it is not difficult in practice except by comparison with the delusive simplicity of the former processes; and therefore that repercolation is better adapted to pharmacopœial use as a model or standard process than any which has yet been tried.

Third. That repercolation may be used on a scale as small as 4 or 8 ounces, by great care and skill, but is not very successful with less than an avoirdupois pound of material for each percolation.

Fourth. That powders for percolation should not be finer than No. 60 for hard compact substances, nor coarser than No. 40 for more loose and spongy substances, with a few special exceptions.

Fifth. That the menstruum should be so adjusted as to dissolve out the medicinal principles with the least practical disturbance of their natural relations to each other and to the extractive matters whereby they are rendered soluble and permanent. Next, that the menstruum should contain the smallest practicable proportion of alcohol; and glycerin only when absolutely necessary, as in cinchonas. And finally, that the menstruum should be so adjusted that when the fluid extract represents the drug, weight for weight, it should also represent the drug by not less than 90 minims to the 100 grains, or more than 97 minims to the 100 grains, since by repercolation the exhaustion is never less than 90 per cent. and perhaps rarely more than 97 per cent. of the total soluble matter.

Sixth. That the powder be moistened with as much liquid as it can be made to hold and yet pass through a No. 8 sieve; that it be not tightly packed; and that it be well macerated before starting the percolation.

Seventh. That the rate of percolation be uniform and very slow. At first, for the reserved portion, the percolate in 24 hours should not exceed the weight of the powder; nor need the rate be slower than to obtain the weight of the powder in 48 hours, although as a general rule the slower the rate the better the results. After the reserved portion the rate may be increased gradually so that the last portion be received in about 6 hours. The separate portion of weak percolate should not exceed the weight of the powder.

Eighth. That a good practical exhaustion requires, as a general rule, for the first percolation, with fresh menstruum, that the total percolates should weigh 3.5 times the weight of the powder.

That for the second percolation or first repercolation, the weight should be 4.5 times that of the powder. And for all subsequent repercolations the weight should be 5, 6, or 7 times that of the powder, according to the nature of the substance percolated, and the skill and care with which the process is managed.

Ninth. That the relation of weight for weight, instead of minim for grain, should be established under proper controlling conditions. But that unless properly guarded in the quality and moisture of the drug used, the new relation is liable to be even more inaccurate than the old, because the poorer the quality of the drug the less dense will be the percolates, and the greater will be the volume for the prescribed weight; and this involves the serious difficulty that when the fluid extract is made by weight but administered by measure, the poorer the drug from which it was made the smaller, as well as the weaker, the dose will be.

Tenth. That some good practical method of comparing fluid extracts by a standard is very much needed; and that for such drugs as cinchona, a method of arithmetical dilution would be easy and practical if well worked out.

Whilst the above-mentioned work on cinchona was in progress a paper by Mr. J. U. Lloyd, of Cincinnati, appeared in the *American Journal of Pharmacy*, for 1878, p. 1, upon Fluid Extract of Cimicifuga. This paper contains so many valuable observations, made without bias, and with such care and labor as at once to command attention. The results, however, were in many important respects so at variance with those of the previous experience of this writer as to force upon him the conclusion that Mr. Lloyd might have misinterpreted some of his observations; and if so it was important that his work should be gone over in the light of the many useful suggestions it contains for those who might follow him. It is regretted that he did not refer to later papers on the subject of percolation and repercolation, or at least did not adopt some important modifications that are published in later papers.

His work upon cimicifuga has been repeated by precisely the same method as given above for cinchona, that is, in accordance with the later experience on percolation and repercolation, and the results are given. Those who will compare these results with those of Mr. Lloyd will find important discrepancies which must belong to one set of observations or the other. On one important point Mr. Lloyd must reach a wrong conclusion, for it certainly can be demonstrated, upon well-known physical laws, that maceration to a proper extent is useful and necessary to other conditions of the problem. This point is so well established by general experience that this part of his work was not gone over. The formula and process adopted here were as follows:

Take of cimicifuga, in powder No. 60, ... 32 parts.
Stronger alcohol, s. g. .819 at 15.6° C. (=60° F.),
or s. g. .811 at 25° C. (=77° F.), a sufficient quantity.

Moisten 8 parts of the cimicifuga with 2 parts of the alcohol, and pack it firmly in a percolator. Then pour alcohol on top until the moist powder is thoroughly filled with liquid and the air is forced out; cover the percolator and macerate for 48 hours. Then arrange the percolation for an automatic supply of menstruum, and start the percolation at such a rate as to give about 1 part of percolate every 3 hours. Reserve the first 6 parts of percolate, and continue the percolation to practical exhaustion, receiving the weaker percolate in separate portions of about 4 parts each.

Then moisten a second portion of 8 parts of the cimicifuga with 2 parts of the second percolate from the first portion of powder, pack it firmly in a percolator, and supply it on top, first with the remaining 2 parts of the second percolate from the first portion, and then with the successive weak percolates in the order in which they were obtained, until the moist powder is entirely filled with liquid. Then macerate for 48 hours, and percolate to practical exhaustion at the same rate as in the first portion of the cimicifuga, using first the weak percolates in their proper order, and then fresh menstruum. Reserve the first 8 parts of percolate, and receive the weak percolate in separate portions of about 4 parts each.

Then moisten a third portion of 8 parts of the cimicifuga with 2 parts of the second percolate from the second portion of the cimicifuga, and conduct the percolation in exactly the same manner as in the second portion, reserving the first 8 parts of percolate.

Then moisten the remaining 8 parts of the cimicifuga for a fourth percolation, and conduct it in exactly the same manner as the second and third portions.

Mix the four reserved percolates, weighing 30 parts, and set it by as finished fluid extract of cimicifuga; and having properly labelled and numbered the separate portions of the weak percolate, set these by until the process for making this preparation is to be resumed; and then use them exactly as in the second, third, and fourth percolations, reserving 8 parts of the first percolate from each 8 parts of powder as the finished fluid extract, ever after, and setting aside the weak percolates from each operation to be used in the next succeeding one.

In applying this formula and process each part was represented by a troy ounce, and therefore the percolations were made with 8 troy ounces of powder each. For the purposes of this trial the percolate was separated in portions of about 2 troy ounces or 62 grams each, instead of 4 troy ounces as indicated in the process, and each separate portion was carefully weighed. A cubic centimeter of each portion of percolate was carefully weighed on a flat watch glass, and then dried and the dry extract weighed. Then a proportion was made by calculation from these data to find the total dry extract in each portion of the percolate, this proportion being as follows: As the weight of the c. c. of percolate is to the weight of dry extract which it yields, so is the whole portion of the percolate to the dry extract it contains. Having thus obtained the total dry extract contained in each portion of percolate, the sum of these would be the total extract of all the portions. But as these portions varied in weight the series would not represent the rate of exhaustion. Therefore another proportion was made to show the rate or progress of exhaustion by the percentage of dry extract contained in each portion of percolate. The formula for this proportion is as follows: As the weight of the portion of percolate is to the weight of dry extract which it contains, so is 100 to the percentage of the dry extract contained in the portion of percolate. The difference of specific gravity between the menstruum and the percolate, which also shows the rate of exhaustion, was obtained by a small sp. gr. flask.

The following table gives the detail of these observations in compact form, but, as it was found by examination of the residue that the strong alcohol did not fully exhaust the cimicifuga, the percolations were only carried as far as the third, at which point it was determined to try a new menstruum, in another process.

The first percolation of the table being simply a percolation with fresh menstruum to practical exhaustion, serves to compare and check the other percolations in their results. The 8 troy ounces of cimicifuga = 248.8 grams required 845.33 grams of percolate for practical exhaustion, though this was short of actual exhaustion. The total percolate is therefore nearly three and a half times the weight of the powder, and is as little as will give a practical

CIMICIFUGA WITH STRONGER ALCOHOL.

Portions of Percolate.	First Percolation				Second Percolation.				Third Percolation,			
	Grams. Weight of Portions of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.*	Difference of Sp. gr.	Grams. Weight of Portion of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.	Difference of Sp. gr.	Grams. Weight of Portion of Percolate.	Grams. Weight of Dry-Extract.	Per cent. of Dry Extract.	Difference of Sp. gr.
1st.	62.20	7.78	12.51	.0444	63.41	12.15	19.16	.0636	61.22	10.98	17.93	.0556
2d.	65.35	6.25	9.56	.0380	64.23	8.08	12.58	.0440	66.35	8.53	12.86	.0476
3d.	64.51	4.84	7.50	.0264	63.12	6.82	10.80	.0328	64.30	6.97	10.84	.0372
4th.	63.08	3.36	5.33	.0232	62.54	4.22	6.74	.0240	55.00	4.79	8.71	0652
5th.	61.22	2.30	3.76	.0184	61.65	3.54	5.74	.0204	62.00	4.32	6.97	.0272
6th.	60.24	1.69	2.80	.0140	62.36	2.90	4.65	.0164	62.22	3.38	5.43	.0224
7th.	61.00	1.30	2.13	.0116	63.11	2.63	4.17	.0128	63.34	2.76	4.36	.0184
8th.	60.02	1.29	2.15	.0108	63.41	2.21	3.49	.0104	62.24	2.51	4.03	0148
9th.	65.37	1.11	1.70	.0096	62.12	1.76	2.83	.0068	62.56	2.18	3.48	.0124
10th.	61.86	1.11	1.79	.0028	62.32	1.58	2.46	.0044	63.06	1.98	3.12	.0096
11th.	112.52	.91	.81	.0036	62.24	1.39	2.23	.0060	64.02	1.80	2.81	.0100
12th.	108.01	1.25	1.16	.0016	63.33	1.16	1.83	.0044	63.44	1.68	2.65	.0100
13th.	.....	.....	.....	.....	80.01	1.77	2.21	.0060	62.32	1.20	1.92	.0082
14th.	.....	.....	.....	.....	98.00	1.90	1.94	.0052	66.80	.90	1.35	.0018
Totals	845.38	33.19	.....	.....	931.85	52.06	.....	.....	878.87	53.89	.....	.....
Reserved Extract	....	18.87	.....	.....	.....	31.27	.....	.....	.....	31.27	.....	.....
Extract carried forward	.....	14.32	.....	.....	....	20.79	.....	....	.....	22.71	.....	...
Extract from each Percolation	.....	33.19	.....	.....	.....	37.74	.....	.....	.....	33.19	.....	.....

exhaustion of this drug with this menstruum. This is more than double the proportion of the officinal U. S. P. formula, and accounts for a part of the defects of the officinal preparation. The extract obtained by this first percolation of the table is 33.19 grams or (248.8:33.19::100:) 13.34 per cent. of the weight of the powder. Then as these percolations were made by repercolation, the total extract should be (33.19 × 3 =) 99.57 grams. But the total obtained (33.19 + 37.74 + 33.19 =), 104.12 grams, slightly exceeds this, showing that the total exhaustion was rather better than the first of the series.

Now if the total extract to be expected from the 24 troy ounces = 746.4 grams of powder be 99.57 grams, and as the finished fluid extract is to weigh only (6 + 8 + 8 =) 22 troy ounces = 684.2 grams, then the extract which should be contained in the reserved portions which constitute the finished fluid extract should be (as 746.4 : 99.57 : : 684.2 :) 91.27. But really the total extract in these reserves is only (18.87 + 31.27 + 31.27 =) 81.41 grams, or

10.16 grams less than it should be. This deficit is mainly due to the process having been stopped at the third percolation instead of being carried on to include the fourth. In order that the fluid extract should represent the drug, grain for grain, or weight for weight, if the extract was all of equal medicinal value, the reserved percolates should weigh 186.6 + 248.8 + 248.8 grams, and should contain 24.9 + 33.19 + 33.19 grams. This fluid extract, to have represented the drug in the relation of minim for grain should have measured (177.12 + 236.16 + 236.16 =) 649.44 c. c., but it really measured 676 c. c., and therefore the minim did not represent the grain ($\frac{649}{676}$) though the preparation is much stronger than the officinal one which purports to have this relation.

To endeavor to remedy the apparent defects of this process and make a preparation which shall more nearly represent the entire drug, another set of repercolations was made with a new menstruum. As the officinal menstruum, namely, stronger alcohol, did not fully exhaust the drug, and separated out the resinous portions from their natural associates and solvents in the drug, the attempt was made to go to the other extreme and try a solvent or menstruum which should contain perhaps too little alcohol, and if so, yield a preparation overloaded with extractive matter, so that by comparing the results of the extremes, a better menstruum than either extreme might be found. With this object the new menstruum was made of equal parts (by weight) of stronger alcohol sp. gr. .819 at 15.6° C. (= 60° F.), or .811 at 25° C. (= 77° F.) and water. This mixture required 26.5 f℥ of water to 2 pints of stronger alcohol. The sp. gr. of this mixture is .926 at 15.6° C. (= 60° F.), or .919 at 25° C. (= 77° F.), or .9236 at the room temperature at which the weighings were made.

The same formula and process were used as in the first repercolations of cimicifuga, with the exception of the menstruum, and the powder was from the same stock, and used on the same scale of a troy ounce = 31.1 grams for each part, and therefore 8 troy ounces = 248.8 grams of powder for each percolation; and in this case the whole four percolations were made. The following table gives the results of this repercolation, and contains the same elements obtained in the same way, but the first percolation attained a much more thorough exhaustion, while the subsequent ones were not carried so far on account of the apparent inertness of the extractive matter obtained. The third percolation was much less successful than the others in consequence of too short a ma-

CIMICIFUGA WITH NEW MENSTRUUM.

Portions of Percolate.	First Percolation. Grams. Weight of Portion of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.	Difference of sp. gr.	Second Percolation. Grams. Weight of Portion of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.	Difference of sp. gr.	Third Percolation. Grams. Weight of Portion of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.	Difference of sp. gr.	Fourth Percolation Grams. Weight of Portion of Percolate.	Grams. Weight of Dry Extract.	Per cent. of Dry Extract.	Difference of sp. gr.
1st	69.18	23.55	34.04	.1212	67.78	22.56	33.29	.1104	64.67	16.89	26.12	.0948	67.55	24.53	36.31	.1324
2d	70.72	19.45	27.50	.0944	64.59	15 65	24.23	.0824	64.22	14.58	22.70	.0808	65.07	21.10	32.58	.1148
3d	66.88	13.27	19.70	.0716	65.07	15.14	23.27	.0800	66.17	13.13	19.84	.0728	57.92	15.28	26.38	.0928
4th	64.34	9.72	15.10	.0548	69.16	14.08	20.36	.0700	66.67	11.62	16.00	.0636	58.70	13.06	22.25	.0820
5th	64.55	7.12	11.03	.0408	76.12	12.26	16.11	.0556	65.90	9.85	14.95	.0536	53.84	7.29	13.54	.0684
6th	62.34	4.48	7.18	.0312	63.78	7.92	12.43	.0452	60.43	7.45	12.33	.0432	60.49	9.25	15.29	.0560
7th	62.31	3.19	5.12	.0248	65.14	6.25	9.58	.0372	90.10	8.63	9.05	.0344	65.68	8.24	12.55	.0480
8th	83.27	2.52	3.03	.0160	64.50	5.98	9.27	.0348	56.89	4.40	7.73	.0294	58.34	6.84	11.72	.0452
9th	107.39	.93	.86	.0080	88.97	5.21	5.85	.0244	69.75	5.25	7.53	.0268	66.88	7.36	11.01	.0436
10th	56.52	.46	.81	.0072	65.08	2.35	3.61	.0176	53.83	3.64	6.77	.0248	65.17	6.03	9.25	.0384
11th	65.64	.18	.27	.0096	64.43	1.70	2.64	.0138	62.49	3.36	5.38	.0176	59.91	6.05	10.09	.0364
12th	63.91	.03		.0044	64.43	1.49	2.31	.0118	63.66	4.17	6.55	.0216	63.99	5.21	8.14	.0332
13th	121.02	.06		.0056	63.94	1.54	2.41	.0086	54.35	2.67	4.91	.0168	63.68	4.51	7.08	.0350
14th					63.94	1.10	1.72	.0066	112.57	5.88	5.22	.0196	61.60	3.43	5.57	.0296
15th					63.80	1.01	1.51	.0038	63.57	3.00	4.72	.0172	59.70	2.97	4.98	.0204
16th					39.59	.68	1.70	.0026	63.57	1.99	3.13	.0172	67.18	2.19	3.26	.0132
17th									89.14	2.90	3.25	.0156	63.10	1.05	1.66	.0108
18th													61.86	.99	1.60	.0064
19th													100.86	1.14	1.13	.0032
20th													67.11	.58	.86	.0040
Total	958.57	84.96			1050.22	114.92			1167.98	119.41			1287.98	147.03		
Reserved Ext.		56.27				67.43				56.22				73.97		
Extract carried forward.		28.69				47.49				63.19				73.06		
Ext. from each Percolation.		84.96				86.23				71.92				73.84		

ceration. This carried too much of the extract forward by the weak percolates into the fourth percolation, and overloaded it But this serves as an excellent example of the way in which the errors of one percolation are corrected by those which follow when repercolation is used.

The first percolation of 8 troy ounces (=248.8 grams) required a total percolate of 958.57 grams for exhaustion, or nearly 4 times the weight of the powder, and gave 84.96 grams of extract, which is 34.14 per cent. of the weight of the powder. The 32 troy ounces (=995.33 grams) of powder should therefore give (84.96×4 =) 339.84 grams of extract. But when the extract actually obtained from the four percolations is summed up, it is found to be only (84.96+86.23+71.92+73.84=) 316.95 grams, or 22.89 grams less than the indicated quantity. This is, therefore, an apparent loss of (as 995.33 : 316.95 : : 100 : 31.84, and 34.14—31.84=) 2.3 per cent., which considering the apparent quality of final extracts in repercolation, is quite unimportant, at least in view of the far greater deficiencies of the officinal processes, or any modification of them hitherto used.

Now if each troy ounce of powder is to be represented by a troy ounce of the fluid extract, and the fluid extract be adjusted to the solid extract obtained, then the reserved percolates should weigh, respectively, 186.6, 248.8, 248.8, and 248.8 grams, and should contain 59.41, 79.22, 79.22 and 79.22 grams of extract. But by the table the reserves weigh 206.76, 266.60, 261.73, and 249.24, and contain 56.27, 67.43, 56.22, and 73.97, thus making a very imperfect exhibit, though still far ahead of the present or past officinal processes. The conditions being new, each percolation was varied in management in order to reach the best method. This was not reached until the fourth percolation, and one or two more percolations, using much more liquid to moisten the powder, would have been needed to obtain greater precision and uniformity. The total finished fluid extract, which should represent 30 troy ounces (=933 grams of the drug), when made to bear the relation of minim for grain, weighed 984 grams, and was, therefore, considerably too heavy. This, and the tendency of the percolate to become overloaded with extractive, at the same time that it illustrates the value and appropriateness of the principle of repercolation, also shows that this new menstruum has too little alcohol, and leads to the inference that a menstruum of 2 parts stronger alcohol and 1 part water would be better adapted to cimicifuga than either of the extremes here tried. Such a proportion would, by repercolation, probably yield a fluid extract which, in the proportion of weight for weight, would also have the proportion of minim for grain, or what would represent the drug better because more accurately than by any known method of percolation, including repercolation, namely, 90 to 97 minims for each 100 grains of the drug. In readjusting all fluid extracts, therefore, to bear the relation of weight for weight to the drug, the weight should measure in minims from 90 to 97 minims for every 100 grains, to make the therapeutic value of the minim and grain and of the fluid extract and the drug practically equal. This can be readily done by variations in the menstrua used, but not without the expenditure of much time, skill, and labor, an amount which no individual or committee can afford to give, but which a Pharmacopœia must have in order to be respected as a standard. It may be mentioned in illustration of this point that all the time and labor that the writer could possibly spare, including at least three evenings of every week, for three and a half months, has been given to this paper, which embraces only two fluid extracts, neither of which are yet in the condition they should be for the Pharmacopœia for want of more time and labor.

It now remains to give some account of the mechanical contrivances which, in the hands of the writer, seem best adapted to a uniform and practically good exhaustion of the soluble portions of drugs without the use of heat, so that the fluid extract of the drug shall bear a tolerably definite and uniform relation to the drug of minim for grain and weight for weight, for the writer now believes that both these relations can be had at once with a practical and sufficient degree of accuracy; or with accuracy enough for the present relations of pharmacy to therapeutics. It can hardly be doubted that by a competent knowledge of known physicial laws, and by a fair application of this knowledge to the problem, a fluid extract can be made by repercolation, without heat, bearing the proper relation, with great accuracy, but the success or want of success with which this is done will vary much more with the degree of knowledge and skill applied to it, than with any particular form of apparatus used. That is, the measure of success will always be in the application of well-known physical laws. The writer, therefore, desires to guard against any misleading effect of a simplicity that is not intended to be *ad captandum,* for it would be very hurtful to continue in the present to underrate a problem which has been so very much underrated in the past. If the principles involved, and the difficulties of carrying them out, be once fairly comprehended, the mechanical appliances may be easily varied; and yet must still leave some one contrivance as the best until a better be found.

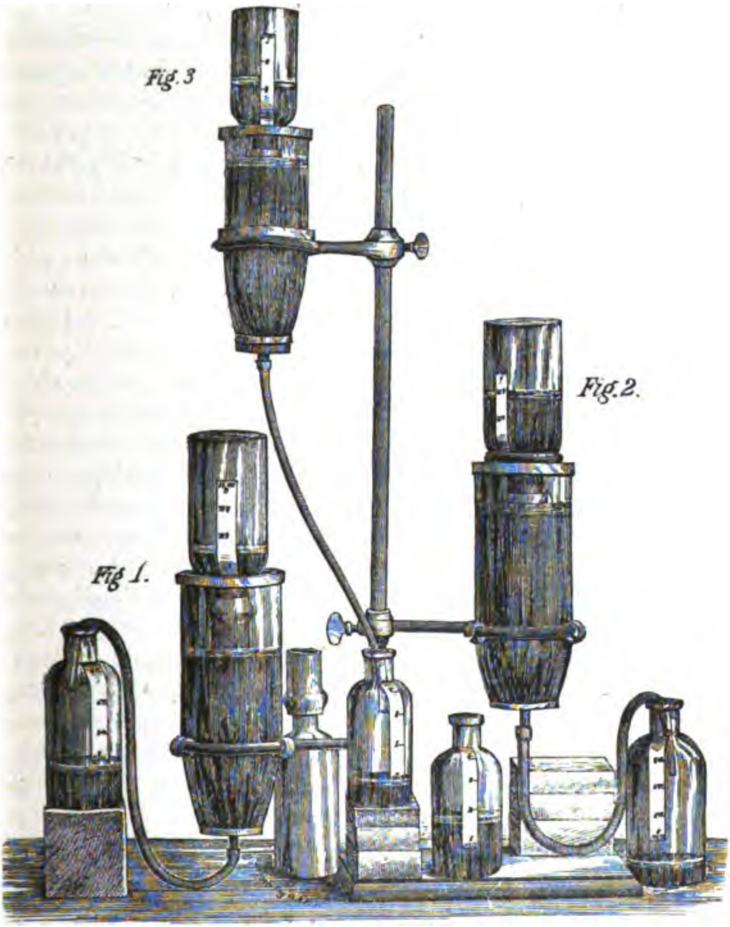


Fig. 3
Fig. 2.
Fig 1.

Scale, one-sixth of the actual linear size.

No better form of apparatus has been found by the writer than that which has now been used, upon various scales, during the past twelve years, an account of which was published in 1872, and which is reproduced with improvement and amplification in this paper. To simplify this apparatus with the slightest possible sacrifice of the principles involved, with the object of getting the principles to be better and more generally understood and applied where so much needed, is the object of introducing the modified apparatus shown in the cut.

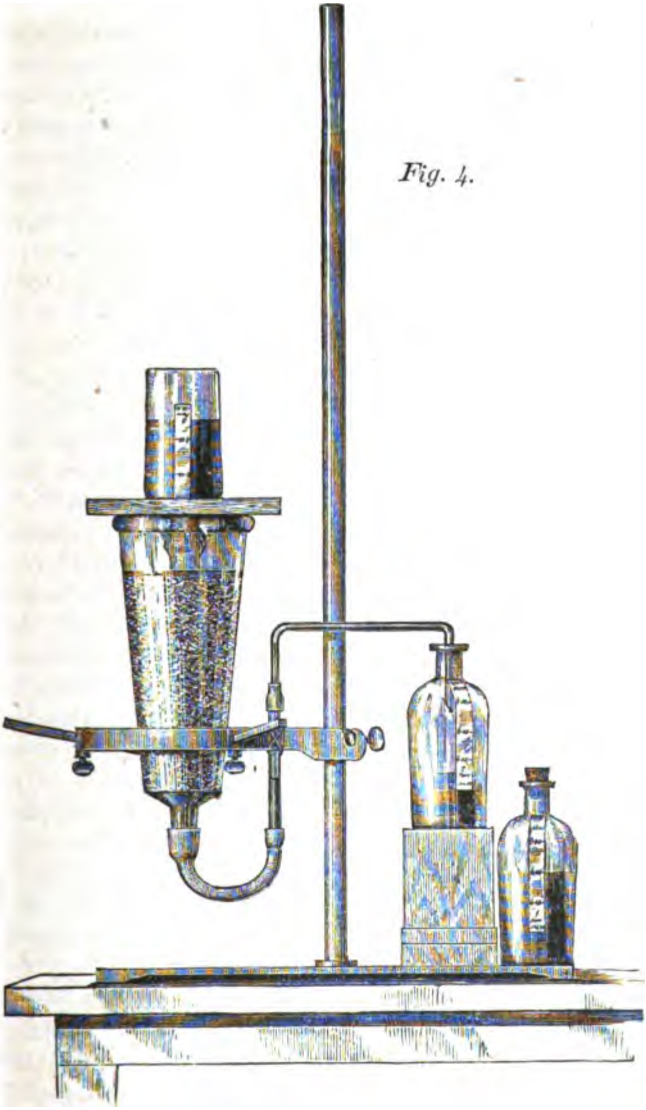
The cut presents three separate groups of apparatus in positions to illustrate three states of repercolation, and it is to be understood that all intermediate positions are often useful and necessary even in the same percolation. The support is a common apparatus stand, the rings of which are reduced to the proper size by short sections of rubber-tubing cut open and placed on the wire of the ring when needed; or, a section of larger tubing stretched over the percolator as in Fig. 3. The percolators are common lamp chimneys, costing about five cents each, and are of the size and form known technically as "A" and "B" "Sun Chimneys." These are of very good form, though not the best—for percolators, and should be selected with as small an opening for the stopper as possible, and with the smoothest, thickest, and most regular edge, since it is practically impossible to stop some of their irregular edges tightly. The smallest size, Fig. 3, holds conveniently 4 ounces of most powders, and the larger holds 8 ounces—to the points shown in the cut. A good soft cork, bored in the centre for a short piece of glass tube of not more than ⅛th of an inch or 3 mm. bore, serves to close the small end of the chimney. A rubber cork is best, and such may be made of concentric sections of rubber tubing of different sizes; or the largest cork at hand may be increased to the proper size by stretching around it short sections of rubber tubing. The short piece of glass tubing should not go quite through the cork on the inside, and should project about an inch=25 mm. outside. A piece of rubber tubing of not over ⅛th inch (=3 mm.) bore, and about 13 inches (=.325 m.) long, has one end slipped on to the glass tube. If this tubing be much larger than the dimensions given it fails to be filled with the liquid, and then, when the percolator is in the position of Fig. 3, it fails to perform the office of a Sprengel pump in exhausting the liquid and air-bubbles from the lower part of the percolator. Two disks of blanket or thick flannel, and one of filtering-paper, cut a little larger than the inner surface of the cork, and laid upon it, complete the arrangement of the percolator. The powder, moistened with great care and uniformity, is packed loosely, firmly, or very firmly, according to its nature or condition, with the square end of a stick, say .8 inch (= .02m.) diameter. As a rule the largest practicable proportion of liquid should be used in moistening the powder, because then the powder occupies the smallest space in the percolator, requires the loosest packing, and is saturated for the maceration by the smallest additional quantity of liquid, and therefore gives the most concentrated first percolate for the reserve, and secures the most rapid exhaustion by the smallest quantity of liquid. A disk of filtering-paper is placed on the surface of the powder, of such size that the edge is reflected up against the glass. A disk of board, card-board, or, better, of thick sheet rubber, with a central hole 1.5 inches (= .037 m.) in diameter, is used for a cover. A stratum of liquid, maintained at a uniform thickness of .25 inch (= .006 m.) should cover the powder from first to last, so that it may not drain and contract, or admit air; and this is best maintained by an inverted bottle of the supply liquid, as shown in the cut. The length of the neck and mouth of such bottle may be conveniently elongated when needed, so as to regulate the depth of the stratum of liquid above the powder, by stretching over it a short section of rubber tubing in the manner shown in the first group of the cut, Fig. 1. When the percolator is charged and ready for maceration the small rubber tube is turned up and fastened with a piece of thread or rubber band, so that the end is considerably above the level of the liquid in the percolator, and in so adjusting it care must be taken not to close the tube, because as the liquid descends through the powder to fill up all the interstices it is important that the interstitial air should have a free exit by the tube.

The bottles for receiving the percolate are common round-shouldered prescription bottles, 4 oz. for the small percolator, 8 oz. for the larger. A strip of paper should be pasted lengthwise of the bottle, and at the lower end of this the tare should be marked. It should then be graduated to the quantities desired by weighing into it the proper quantity of water and marking at each level if more than one be desired. This graduation simply serves as a reminder to know when to try the bottle on the scale, for whether the finished fluid extract be adjusted weight for weight, or by an arbitrary weight in each case so as to get the relation of minim for grain, this must equally be done by weighing.

It is convenient to have 6 to 10 of such bottles, and then as soon as 4 are filled from one percolation another can be started. and thus relieve some of the bottles for use over again. The bottles should be numbered from 1 to 10, to keep the proper order of using them, and if more than one series is in use at the same time the second should be designated by the first letters of the alphabet instead of numbers. The maceration should never be less than 48 hours, and a longer time does not seem to be of any use unless the powder be coarse and of hard particles. When the percolation is to be started the percolator is raised to the position of Fig. 3, and the end of the exit-tube placed in the bottle marked for the reserved percolate, for 10 or 15 minutes, in order that the bubbles of air may be driven out and the tube to be filled solid with liquid. As soon as this condition is attained the percolator is lowered to the position of Fig. 1, and the receiving bottle is then to be adjusted higher or lower until a rate of dropping is established of not more than one drop per minute on this small scale; and one drop every two minutes makes a better rate for such quantities. Indeed the rule for all percolation is, the slower the rate the more perfect the exhaustion, and with a smaller quantity of menstruum.

This slow rate and the automatic supply by the inverted bottle admit the process to go on night and day, but if it be desired to go slower, that a mark may not be passed in the night, the bottle has only to be raised or the percolator lowered a little; or by a still greater change of levels the dropping may be stopped altogether. On rare occasions, when dropping at a uniform rate, it will stop altogether, or become very slow. This is in consequence of a bubble of air getting over the orifice of the glass-tube inside and acting as an obstruction. If the tube be moved from side to side, the air-bubble will be started and pass down, and the rate of dropping be resumed. If not thus dislodged, it will most certainly be by raising the percolator for a short time into the position of Fig. 3. With some powders, and some degrees of moistening and packing, the proper rate of dropping will require the position of Fig. 2, and in some stages of many percolations this position will be required; while, if for want of skill and experience the packing be too hard, the position of Fig. 3 may be needed from the first. But the best percolations are those obtained by the position of Fig. 1, where the whole mass is in the equilibrium of maceration, and the fluid all moves downward together at a very slow rate. As the more concentrated portions of the percolate get through, the rate of dropping increases for any position, and occasionally, with loose packing, the position has to be altered to check it. But after the reserved portion has been received, and the quantity required to moisten the next powder, the rate of dropping may be doubled without much harm, and thus half the time be saved.

The slow and uniform rate of dropping is the important point to be attained, and the various positions are simply means of accomplishing this. It is easy to obtain complete exhaustion. That is, a percolate almost colorless and tasteless, and having the same specific



Scale, one-sixth of the actual linear size.

gravity as the menstruum; and how far short of this to stop the process cannot be indicated. But upon this small scale, the percolate from the first portion should weigh from three to four times the weight of the powder, and in the repercolations from five to seven times the weight of the powder. And then, with fair exhaustion each time, the results must continually check each other and improve until, after ten or twelve repercolations, a nearly mathematical accuracy must be attained, and ever after be maintained, all the variation being in the quality of the drug used. The writer has many series of repercolations, on various scales of quantity, which were started five years ago, and suspended from one season of the fresh drug to another, but never interrupted to begin anew, and such would go on indefinitely and with entire uniformity of result if the drugs could be obtained of a quality as uniform as is the process.

Should this method by repercolation become officinal, or come into general use, the apparatus-makers would soon supply a flat-bottomed glass percolator and cover of better form than the lamp chimneys, and of all sizes, at moderate prices. If so, no better form could be adopted than that shown in the preceding cut, if the bottom be flat or very nearly so, and the exit-tube be of the proper size to receive a No. 5 vial cork. Then such a cork bored to receive a piece of glass tubing 1.6 inch (= .04 m.) long, with about 3 mm. bore, would adapt it to the small rubber tubing used with the lamp chimneys. Even with the glass percolators now in common use, a short section of small rubber tubing serves as a cork to go inside the outlet, and the short piece of glass tubing through that. Then the small rubber tubing is used exactly as with the lamp chimneys.

The chief object of presenting this illustration is to show a convenient way of applying the principles involved in the siphon percolator, Fig. 5, to the glass percolator in common use, in order to try to tempt those who have such percolators to use the method in percolation and repercolation. The cut is so plain and so easily understood that it needs but little explanation. The percolator is shown in the position of having been stopped for the night, lest the receiving-bottle should be filled beyond the proper mark. The siphon here is made in two parts, one end of the upper part being telescoped within a larger piece of glass tubing, and the junction made tight by a short section of rubber tubing, through which the smaller tube is free to slide. During maceration, or when the percolation is arrested, the upper part of the siphon is drawn up until the liquid will no longer flow over into the bottle, and the height at which this column of liquid ceases to flow over is a measure of the comparative density of the liquid within and without. As seen in the cut, the liquid will not flow over into the bottle, although the column is several inches short of the height of the liquid in the percolator. But as exhaustion progresses, and the liquid in this column becomes less dense, its counterbalancing height becomes greater, until finally, when the powder is exhausted and the liquid within and without is of the same density, the column rises to the level of the liquid within the percolator minus the friction and capillarity. When the percolation is to be started, the siphon is simply pushed down through the rubber until the liquid flows over, and then the rate is established by carefully raising or lowering the siphon. This sliding-joint, for varying the length of this column of liquid at will, being understood, the other details are plain enough, whilst the charging and the general management are the same as in the smaller and larger percolators.

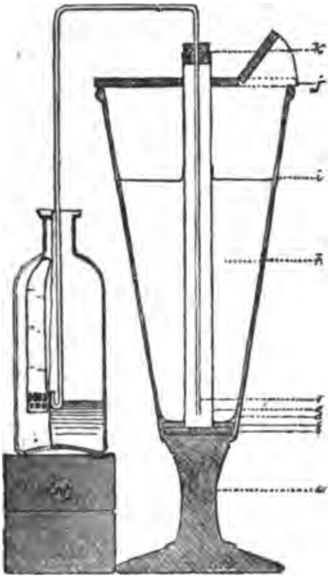


Fig. 5.

Scale, one-sixth of the actual linear size.

However attractive the simplicity of the lamp chimney arrangement may appear it does not yield so good results as the form of percolator reproduced here, with slight improvements, on this page, Fig.

5, from the "Proceedings of the Amer. Pharm. Asso." for 1872, p. 182, for several reasons. First, because the principles involved are not so well carried out, and secondly, because the quantity of substance operated upon is too small. Very good and uniform results need hardly be looked for when the quantity operated on for each percolation is less than an avoirdupois pound. That is, when less than that quantity is used, great care and skill are necessary to get good results. Another percolator, Fig. 6, applying the same principles by the same details, but having about five or six times the capacity of the first, was soon after made and put into use, and cuts of these two percolators are shown upon the preceding and the opposite page, of their relative sizes, both upon a scale of one-sixth of the actual linear dimensions, the reference letters denoting the same parts in both. Of course the principles involved when once understood can be applied to vessels of any kind and size by means of common glass tubing, and in order to have these principles tried by less prejudiced persons than the writer, the mechanism will now be given as plainly as possible, as applicable to this best form of apparatus.

The percolator, *a*, is of the form of the more modern glass or tin percolators, somewhat funnel-shaped to allow substances to swell without becoming impacted, but having no special angle. The smaller has a glass stem and foot like an ordinary celery glass, and the larger is an ordinary stoneware pot, neither having an opening in bottom nor sides. The smaller is about 16 inches (=40 centimetres) in height, of which height about 4 inches (=10 centimetres) is stem and foot, and is of a proper capacity for 16 to 20 ounces (=500 to 600 grams) of material and a proper stratum of menstruum. The bottom, internally, should be about 2 inches (=5 centimetres) in diameter and should be flat, not cup-shaped, as the glass-blowers are apt to leave it. A rim of glass is made upon the upper edge or lip, to strengthen it, and this lip is ground off so that the cover may fit accurately, to prevent loss by evaporation. The height of the foot and stem is not a matter of indifference, since if too short it has to be set upon a stand in order that the receiving-bottle may be conveniently changed.

The larger percolator, *a*, is a stoneware pot of about 2 gallons (=7557 c.c.) capacity, 10 inches (=24 centimetres) high and across the top, by about 6 inches (=14.4 centimetres) across the bottom inside, and it will conveniently hold 4.5 to 6.5 pounds (=2 to 3 kilos), and a proper stratum of menstruum. When to be used for a variety of substances in succession such pots should be well burned and well glazed, to prevent the liquids from getting into the body of the ware.

A disk of blanket, *b*, is cut of such a size and shape as to lie flat upon the bottom, and cover it entirely. Another disk of the same material, but a little larger, *c*, is made with a crucial incision in the centre, so that it may be stretched over the end of the well-tube, *e*. The central or well-tube, *e*, is a simple piece of glass tube about 12 inches (=30 centimetres) long, by .5 to .75 inch (=1.5 to 2 centimetres internal diameter, irregularly notched, or gnawed off obliquely at the lower end. One end of this well-tube, *e*, is pushed through the crucial cut in the centre of the upper disk of blanket, *b*, and the blanket is pushed to the other end of the tube,

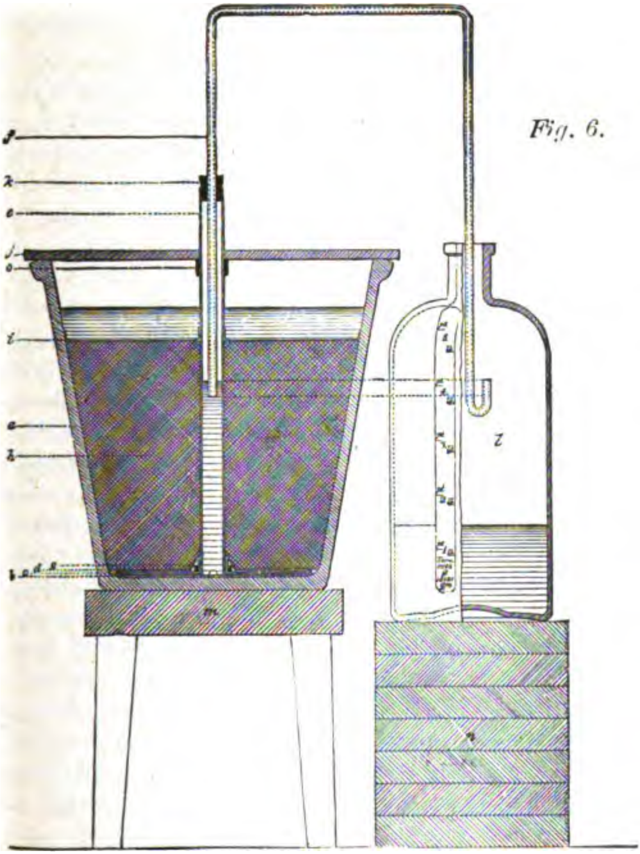


Fig. 6.

Scale, one-sixth of the actual linear size.

so that the corners made by the crucial cut are reflected up against the outside of the tube. These corners are then tied firmly to the tube by passing twine around them, or, are secured by a stout rubber band, *g*, made of a section of rubber tubing of proper size. A disk of filtering-paper, *d*, larger than the upper blanket, *c*, with a crucial cut in the centre, and nicked round the edge so as to lie flat against the sides of the percolator where reflected up against them, is pushed down upon the upper blanket, the well-tube passing through the crucial cut in its centre.

If now a piece of paper be twisted round the upper end of the well-tube, or a cork be temporarily stuck into it, to keep out the moistened powder, the percolator is ready to receive its charge, which is packed around the well-tube and upon the disks of paper and blanket so as to occupy the main body of the percolator, *h*, up to about the position of *i*.

When the charge, having been properly moistened, rubbed, and sifted, so as to be entirely uniform and free from wet lumps, is packed around the well-tube loosely or firmly, according to the nature of the substance and the menstruum, its surface is covered by a disk of muslin or paper, *i*, cut so as to lie flat and smoothly upon the surface. The object of this is to distribute the menstruum as it is poured on, and to prevent the stream from breaking up and deranging the surface. Should this disk show a tendency to float in the stratum of menstruum it may be weighted down by a few fragments of glass. The percolator is then ready to receive the menstruum or weak percolate, and a stratum of the liquid should be carefully kept covering the entire surface well until the whole mass of the substance to be percolated is entirely saturated. The cork is to be taken from the well-tube before the liquid is poured on, and then the liquid will pass down into the substance like a piston, pushing the interstitial air down before it to pass out through the blankets and the well-tube; and finally the liquid will rise in the well-tube until its surface is within an inch or so of the surface of the liquid outside.

The whole substance is now in a perfect condition for maceration, and the surface should be left covered with the liquid to the depth of at least .4 inch (= 1 centimetre). In the larger percolator a short section of rubber tubing, *o*, is stretched over the upper end of the well-tube, and slipped down so as to support the centre of the cover. A tightly fitting cover, *j*, made of sheet rubber .25 inch (= 6 millimetres) thick, with a hole in the centre for the well-tube, is then put on. If made of sheet rubber this cover fits so closely that it will soon save its cost by preventing loss of alcohol by evaporation. Its size in the larger percolator permits one side to be bent up when liquid is to be poured in. But in the smaller percolator it is very convenient to have one side of the cover cut two-thirds through from below, as shown in the cut, the undivided portion forming a good spring hinge permitting this part of the cover to be easily raised to pour on liquid. If a self-feeding bottle be used, as is generally advisable in order to keep the level of the liquid constant and thus obtain a flow at a uniform rate, it may be easily applied by making a hole of suitable size in the cover. When thus supplied and covered the maceration should continue for 48 hours at least. The whole arrangement now represents a well, dug in the wet soil of the substance to be percolated, and the proposition is, to pump out this well at so slow a rate that the liquid from outside the well coming in to supply that rate, through the disks of paper and blanket, which represent the gravel stratum of the soil, may descend so very slowly as to be nearly frictionless. The object is, to give the whole liquid up as nearly as possible to gravitation, and to so diminish the rate of descent that the particles or portions of liquid which pass between and around the particles of solid matter may travel downward no faster than the portions of liquid which pass through the pores or interstices of the more solid substance whose soluble portions are to be washed out. Because, if the whole mass of liquid travelled downward at absolutely the same rate through a perfectly saturated mass of solid permeable substance partially soluble in the liquid, and if the molecules of liquid passed downward in absolutely straight lines, through some particles, but between others, and always at a uniform rate, it is easy to see that all the first portion of the liquid would come through saturated, and all the remainder would hold nothing in solution, because the substance would be absolutely exhausted by just the quantity of liquid which it was capable of saturating. The writer has on one or two occasions made percolations so slowly as to somewhat approximate this theoretical result. The dropping in one case was not over 4 drops in 24 hours, or about a cubic centimetre every 5 days. To pump out this well at a uniform rate which can be easily controlled, is therefore the most important element in a successful percolation, and the only one which has offered much difficulty in the past. And it can only be effectually done by means of maintaining a difference of levels in the liquid inside and outside of the well-tube The moment a drop of liquid is taken from the well-tube, the liquid outside tends to supply its place, and will supply it in a certain definite time ; and if the entire mass of liquid be under the same tension, and equally free to move through the short distance required at the slow rate required, then as liquids are practically inelastic, every drop throughout the whole mass, whether in the interstices of the solid particles or between those particles, will have moved downward through the distance and at the rate required to supply its share of the drop required to replace the one taken from the well. And if the volume of the drop be compared with the total volume of liquid set in motion, and the rate of its movement as taken out be multiplied into the mean horizontal area of the percolator, a good indication is obtained of the almost infinite slowness with which the vertical columns of molecules of the liquid descend through the mass; and thus the physical laws which govern percolation may be better understood.

The proposition, then, is to keep the total mass under a uniform tension throughout, and to do this by maintaining a difference in levels between the liquid inside and outside the well ; and this difference of levels, which varies with each substance, and with every stage of the percolation of the same substance, is to be maintained by drawing liquid from the well at so slow a rate as to disturb the uniformity of tension throughout the whole mass as little as possible, so as to have the whole liquid in motion at a uniform rate like a slowly-descending piston. Of course, the simplest way of taking the liquid from the bottom of the percolator is the old often-used stopcock in an opening in the bottom, but this proves objectionable for several reasons. First, it is difficult, though not impossible, by means of a stopcock at the bottom, to keep the whole mass of matter at a uniform tension, or in uniform maceration. Channels of liquid in more rapid motion are more apt to form, and the packing has to be much more carefully done in order to prevent this tendency to currents in the mass. Next, in actual practice, it was found that no stopcock could be arranged to do its work automatically according to the natural requirements and varying conditions of each case. It must be arbitrarily set to run at some rate of dropping that would be decided by the judgment of the operator, rather than by the natural conditions and laws of the process. Then no stopcock could be found which would continue to run at so slow a rate of dropping with any degree of uniformity through so long a time. The smallest particle of solid matter would dimish the rate, or stop it altogether, so that it required to be continually watched or readjusted, and every change that was made disturbed the whole of the delicate balances and motions of the process. Again, all the metals of which ordinary stopcocks are made are attacked by the liquids in so long a process, and have the same objection that metallic percolators have. Glass stopcocks were tried, but they were found equally liable to all the objections except the last. This experience led the writer directly to the well-tube, and to the use of a siphon, *f*, as best fulfilling all the conditions required, since it can easily be set lower or higher, to adjust the levels to the desired rate of motion, and having a free flow it works automatically and with certainty. This siphon, *f*, is made of glass tubing, of about .125 inch (=3 millimetres) bore, bent twice at right angles, the two legs being about 12.5 inches (=31 centimetres) long. The outer leg is a little longer that the inner one, and turned up upon itself for about .750 inch (=2 centimetres), as shown in the cuts. The legs should have only such a difference in length that the inner one should reach the bottom of the well-tube when required, and when measured upon the outer one should reach to about midway of the turned-up end of the outer leg. This construction prevents the siphon from emptying itself at any time, for, when the liquid is drawn over by the siphon until the surface of liquid in the well-tube falls to a level with the end of the turned-up portion, as shown by the lines in the cut of the larger percolator, the columns of liquid in the siphon will be of equal length and will counterbalance each other, and therefore the flow will cease without emptying the siphon. But as soon as the level of liquid in the well is raised by fresh additions of menstruum on to the substance, the flow will recommence at a rate proportionate to the difference of levels, and may be readjusted to the required rate by slipping it up or down in the cork, *k*, in the upper end of the well-tube. This cork, *k*, should be bored to fit the siphon so tightly as to hold it in any position, and should have a groove filed longitudinally on its outer side so as to allow free entrance and exit of air to the well-tube. A receiving-bottle, *l*, upon which a strip of paper is pasted to receive any graduation-marks that may be desired, completes the apparatus. The strip of paper on the bottle should have the tare of the bottle in grams and in grains marked in ink at its lower end, and should then be varnished. Then the graduation-marks may be made with pencil, and be rubbed out and replaced as different graduations may be required for different substances, the graduations merely indicating when to try the weight of the accumulating percolate. A wooden stand, *m*, is necessary for the larger percolator to enable the receiving-bottle to be conveniently removed and replaced without disturbing the siphon, and wooden blocks, *n*, are necessary to support the receiving-bottles at various heights. As a general indication, the rate of dropping from the smaller percolator should be about six or eight drops to the minute, and for the larger one about ten to twelve to the minute. But it should always be borne in mind that the rate cannot be uniform without some self-feeding arrangement that will preserve a uniform stratum of liquid upon the surface of the substance, and that, with such an arrangement, the slower the rate the more perfect and the more economical the exhaustion will be. With a rate of two or three drops a minute, the results are practically perfect, when the conditions of fineness of powder and appropriate menstrum are properly fulfilled.

The maceration for at least 48 hours is useful for many reasons, chiefly that the adjustment of temperature and solubility may take place fully and naturally; that the particles may be thoroughly permeated by the liquid, and the liquid become saturated. And because if the maceration be omitted, the percolate, in many cases, will not be entirely bright or clear. Then, as a rule. the longer the maceration, within reasonable limits, the stronger will be the percolate that comes next after the maceration, no matter at what stage of the repercolation the maceration be applied.

When the maceration is completed and the percolation to be started, the siphon is put in place with about three inches (= 7.2 centimetres) of the inner leg immersed in the liquid of the well tube. Then the best way to start the siphon is by means of a piece of glass tubing of the same size as the siphon and any convenient length, armed at one end with a short section of rubber tubing of such size as to slip over the end of the turned-up part of the siphon easily, but fitting tightly, or being tied onto, the end of the piece of glass tubing. The siphon and receiving bottle being now in position to start, the rubber end of the glass tube is passed into the neck of the receiving-bottle and down till the rubber slips over the end of the turned-up portion of the siphon. Then, by gentle slow suction with the mouth at the upper end of the glass tube, the siphon is slowly filled, and when filled the glass tube and rubber are removed. As soon as the dropping commences the siphon must be raised or lowered until the desired rate of dropping is attained. If the siphon has to be raised in order to attain the rate, it must be done little by little, in order to avoid raising the inner end out of the liquid in the well. The rate of dropping can only be established with entire uniformity when the inverted automatic feeding-bottle is used for supplying menstruum, because when the menstruum is poured on from time to time the dropping will be a little faster as the outside level is raised by each addition.

When weak percolates of diminishing strength are successively used on top, the stratum of liquid should be kept thin, so that each stronger weak percolate may have nearly all sunk into the substance before the next weaker one is used. In receiving the percolate, the blocks, *n*, are used to support the receiving-bottle in any position, and when the percolation is to be stopped, or made to go very slowly, during the night, for example, this may be effected either by raising the siphon higher or by blocking up the receiving-bottle so that the outer end of the siphon is immersed in the percolate received to the necessary depth. Of course when the receiving-bottle is blocked up so that the mouth or desired mark upon the bottle, is near the level of the liquid in the percolator, the bottle can never run over nor the mark so raised be surpassed. The dropping end of the siphon should always be inside of the receiving bottle, because thus all loss by evaporation is avoided, the air inside the bottle being still and being saturated. If the same rate of slow dropping was carried on outside in the moving air of a room, and the drops fell into a funnel, for example, about one-fourth of the menstruum would be lost by evaporation, the more volatile portions in greater proportion, and the percolate would be turbid and unfit for use.

The last weak portions of percolate may almost always be pushed through by the careful use of water on top, and in proportion as the operator acquires skill in the management, little menstruum will be lost. When exhaustion is practically complete the siphon is pushed down to the bottom of the well, and the last weak percolate drawn off rapidly.

Then if another portion of the same substance is to be put into the percolator, the exhausted residue should be so removed as not to disturb the disks of paper and blanket at the bottom.

The principles of this process once, well understood, modifications of apparatus will occur to many. The simplest of those that have been tried on a scale larger than the one above shown with lamp chimneys, is to dispense with well-tube and siphon, and replace them with a piece of rubber tubing of small bore. One end of this is placed between the two disks of flannel near the centre of the percolator, and then the tubing is led up through any part of the packed substance, say near, but not against, the side of the percolator, as this would leave channels for liquid, and then out over the edge of the percolator. Then a small bent portion of glass tubing is slipped into the end of the rubber so as to represent the end of the glass siphon. This end can then, by the flexibility and length of the rubber tube, be kept at any desired position. This, however, does not answer as well in practice as the well and siphon, nor does any other yet tried, including the simplification adopted with the lamp chimney, answer as well, when judged by the results obtained.

The writer made a conditional promise at the request of the committee that he would give a table showing his own practice with fluid extracts in regard to the menstruum now used for each, the weight of a pint of the menstruum and the weight of a pint of the finished fluid extract in each case, as bearing upon the proposed new relation of making them weight for weight instead of minim for grain. This table is now offered.

The foregoing part of this paper was originally published in the *American Journal of Pharmacy*, for May, 1878, but for want of time it was not in a complete condition. It was afterwards reprinted from the *Journal* by the author, in pamphlet form, with some additions and corrections, and with some of the tables and other details completed ; but still the subject and the original design of the writer were left incomplete for want of a table of the details of practice by repercolation, which could be supplied from the writer's experience with a large number of the fluid extracts in common use during the twelve years embraced by the paper

As these details embrace the fineness of powders, the menstrua used, the tension of packing, and the weight of the finished fluid extracts ;—and as these details had furnished throughout a number of years a series of the most important fluid extracts, many thousands of pounds of which had been successfully used by the medical profession throughout the United States;—and as the writer had no objection to publishing the results of his experience and labor for the general good of pharmacy and medicine, it was thought to be worth while to complete the paper referred to and offer it to the Association, for the benefit of whose Committee on Revision of the Pharmacopœia the work was originally undertaken. The Association may now, at its pleasure, place the whole or any part of the now completed paper on its records in the Proceedings.

In the following table the first column gives the drugs repercolated.

The second column gives the fineness of powder used ; the number indicating the number of the sieve through which all the powder would pass, coarse and fine together. And the number of the sieve indicates the number of meshes to the linear inch. For example, No. 20 gives a mesh $\frac{1}{20}$th of an inch square less the diameter of the wire, leaving the opening to be, say $\frac{1}{30}$th of an inch. In five cases two numbers are given to indicate that the difference between the coarser and finer particles is much greater than common. The first number indicates the sieve through which the whole would pass. The second that through which the finer portion would pass. In the two articles of cotton-root bark and stillingia the "c. c." of the table means cut and crushed, or torn into short shreds.

The third column gives the menstrua used. All these give good, efficient fluid extracts, but they are not all the best that could be devised through the proper research. Many are results of frequent trials and changes, and many are used in deference to pharmacopœial authority where these are necessary to obtain pharmacopœial results. But where pharmacopœial results are not reached by the menstrua directed, and where they are better reached by different menstrua, those directed by the Pharmacopœia are not used. It is very doubtful whether all those which consist of "Alcohol," would not be better if alcohol of lower strength was used. The many and great advantages of weak menstrua render a thorough investigation of this point very important before the next formulas are adopted.

The "Alcohol" of the table is the U. S. P. officinal, sp. gr. .820.* The "Dil. Alcohol" is the U. S. P. officinal, sp. gr. .928. The "Glycerin" is the U. S. P. officinal, sp. gr. 1.25. The "Acetic Acid" is the U. S. P. officinal, 36 p. c., sp. gr. 1.047. And the "Water of Ammonia" is the U. S. P. officinal, 10 p. c., sp. gr. .960.

All the menstrua are made by weight, and not by measure.

The fifth column gives the proportion of menstruum or of weak percolate which has been found best to moisten the powder properly before sifting and packing. For example, the officinal portion of 16 troy ounces of Aconite Root takes, by the table, 16 troy ounces of menstruum or of weak percolate to moisten it properly before sifting to pack.

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* The alcohol used by the writer has been until very recently stronger as well as cleaner than the U. S. P. officinal "Alcohol," and this has made the weight of the pint of all the fluid extracts which require "Alcohol" as the menstruum, lighter than it would have been if strictly officinal "Alcohol" had been used. The neutral or cologne spirit used rarely exceeds .814 s.g. at 15.6° C. or 60° F., while the officinal "Alcohol" is .820. Now it is the writer's practice to reduce the neutral spirit used as a menstruum to .819 or 820.

The sixth column indicates approximately the pressure to be used in packing the moistened and sifted powder. To make the terms used in the table a little more definite, the following definitions may be useful. "Loosely" means that the moistened powder is put in layer by layer and uniformly distributed with the least pressure upon each layer that will secure entire uniformity throughout, the slight pressure increasing toward the last or upper layer. "Moderately" is intended to indicate a pressure upon each layer that would be about equal to 45 pounds if both hands be pressed upon a scale. "Firmly" is to indicate a pressure of about 60 pounds; and "Hard" means 75 pounds or more.

The last heading of the table, consisting of two columns, gives through an experience of many years of actual practice, the maximum and minimum weights of the pint of finished fluid extract The difference between the maximum and minimum—the menstruum and other conditions being equal, and the exhaustions complete—indicates approximately the quality of the drug used. The average experience of the last three or four years, from greater knowledge, pains and care in selecting, and better facilities for obtaining good materials, gives results which are considerably above the mean of the extreme weights as given in the table, and approximate much more nearly to the maximum weights. Hence this maximum column may be received as the fairest and clearest expression of the practice at the present time. It should not, however, be forgotten for a moment, that the weight or specific gravity of a fluid extract is not by itself any evidence either of the quality of the preparation or of the drug from which it is made. Nor even, if the menstruum be accurately known, is the difference between the specific gravity of the menstruum and that of the finished fluid extract, an accurate measure either of the quality of the drug used, or the completeness of the exhaustion, for it may be very easily seen by a close scrutiny of the tables given in the first part of this paper, that in repercolation the amount of solid matters dissolved out of any drug by a properly adjusted menstruum, does not increase arithmetically with each repercolation, although the active and desirable portions generally do increase arithmetically or nearly so. That is, the weak percolates are none of them as medicinally strong as they seem to be if judged by appearance and by specific gravity. Or, in other words, the weak percolate is a better solvent for the active principles of a new portion of the same drug, than is the new menstruum, even though the specific gravities of the two are greatly different.

FLUID EXTRACTS BY REPERCOLATION.

TABLE OF DETAILS.

DRUG REPERCOLATED.	Fineness of Powder, Sieve Number.	MENSTRUUM USED.	Weight in grains of one pint of menstruum at 25° C.=77° F.	Parts of menstruum or of Weak Percolate to moisten sixteen parts of powder.	How Packed.	Weight in grain of a pint of finished Fluid Extract at 25° C.=77° F.	
						Maximum.	Minimum.
Aconite Root	80	Alcohol.	5908	16	Firmly.	6780	6515
" "	80	Dil. Alcohol.	6727	15	Firmly.	7975	7694
Arnica Root	20	Dil. Alcohol.	6727	16	Hard.	7280	7205
Aromatic Powder	20	Alcohol, 2 parts. Water, 1 part.	6447	11	Firmly.	6760	6718
Asarum	20	Dil. Alcohol.	6727	12	Firmly.	7180	6935
Belladonna Leaf	20	Alcohol, 2 parts. Water, 1 part.	6447	16	Firmly.	7180	6985
Belladonna Root	40	Alcohol, 2 parts. Water, 1 part.	6447	16	Firmly.	7480	7141
Bittersweet	60	Dil. Alcohol.	6727	16	Firmly.	7875	7468
Buchu	40	Alcohol.	5908	9	Firmly.	6500	6360
Buckthorn Bark	20	Alcohol, 25 parts. Glycerin, 5 parts. Water, 70 parts.	7112	12	Firmly.	7825	7640
Butternut Bark	20	Dil. Alcohol.	6727	16	Hard.	7310	7210
Camellia	20	Alcohol, 20 parts. Glycerin, 5 parts. Water, 75 parts.	7165	9	Loosely.	8185	7920
Cannabis Indica	8	Alcohol.	5908	13	Hard.	6888	6253
Capsicum	20	Alcohol.	5908	8	Firmly.	6440	6310
Cardamom Compound	20	Alcohol, 2 parts. Water, 1 part.	6447	16	Firmly.	6781	6710
Cascara	20	Alcohol, 25 parts. Glycerin, 5 parts. Water, 70 parts.	7112	16	Hard.	8023	7010
Cimicifuga	20	Alcohol.	5908	10	Hard.	7143	6940
Cinchona, Yellow	40	Alcohol, 3 parts. Glycerin, 1 part.	6525	8	Firmly.	7785	7610
Cinchona, Yellow, Comp.	40	Alcohol, 3 parts. Glycerin, 1 part.	6525	8	Firmly.	7821	7688
Cinchona, Red,	40	Alcohol, 3 parts. Glycerin, 1 part.	6525	16	Firmly.	7630	7125
Cinchona, Red, Comp.	40	Alcohol, 3 parts. Glycerin, 1 part.	6525	16	Firmly.	7963	7820
Coffee, Green	20	Alcohol, 20 parts.	7165	10	Firmly.	8060	7915
Coffee, Roasted	20	Glycerin, 5 parts. Water, 75 parts.	7165	16	Hard.	7840	7770
Colchicum Seed	30	Alcohol, 2 parts. Water, 1 part.	6447	7	Firmly.	7130	6870
Coca Leaf	20	Alcohol, 1 part. Water, 2 parts.	6943	16	Hard.	7770	7640
Columbo	4–12	Dil. Alcohol.	6727	16	Firmly.	7003	6930
Conium Seed	20	Dil. Alcohol, 86 parts. Acetic Acid, 1 part.	6824	18	Moderately	7872	7230
Convallaria	20	Dil. Alcohol.	6727	10	Firmly.	8185	7968
Cotton-Root Bark	c.c.	Alcohol, 2 parts. Glycerin, 1 part. Water, 2 parts.	7130	16	Hard.	7810	7613
Cubeb	20	Alcohol.	5908	Dry.	Hard.	6423	6350
Cypripedium	20	Dil. Alcohol.	6727	10	Firmly.	7660	7310
Dandelion Root	20	Dil. Alcohol.	6727	10	Firmly.	7805	7625
Digitalis	20	Alcohol.	5908	12	Firmly.	6788	6607
Ergot	30	Dil. Alcohol, 86 parts. Acetic Acid, 1 part.	6824	9	Firmly.	7430	7353
Eucalyptus	20	Alcohol.	5908	16	Hard.	6741	6600
Gelsemium	80	Dil. Alcohol.	6727	16	Firmly.	7286	7210
Gentian	20	Dil. Alcohol.	6727	16	Firmly.	8189	8076
Gentian, Compound	20	Dil. Alcohol.	6727	16	Moderately	7987	7812
Ginger	20	Alcohol.	5908	7	Firmly.	6198	6130
Hops	12	Dil. Alcohol.	6727	16	Hard.	7810	7512
Hydrastis	20	Dil. Alcohol.	6727	8	Firmly.	7508	7408
Hyoscyamus	20	Alcohol, 2 parts. Water, 1 part.	6447	16	Firmly.	7170	6830
Ipecacuanha, U.S.P. process	80	Alcohol.	5908	9	Moderately	7130	6970
Juniper	8	Dil. Alcohol.	6727	Dry.	Hard.	8304	8105

FLUID EXTRACTS BY REPERCOLATION—CONTINUED.

DRUG REPERCOLATED.	Fineness of Powder, Sieve Number.	MENSTRUUM USED.	Weight in grains of one pint of menstruum at 25° C.=77° F.	Parts of menstruum or of Weak Percolate to moisten sixteen parts of powder.	How Packed.	Weight in grains of a pint of finished Fluid Extract at 25° C.=77° F.	
						Maximum.	Minimum.
Leptandra	20	Alcohol, 2 parts. Water, 1 part.	6447	10	Firmly.	7560	7110
Liquorice Root	6–50	Alcohol, 2 parts. Glycerin, 1 part. Water, 7 parts.	7237	14	Hard.	8395	8008
Lupulin		Alcohol.	5908	Dry.	Loosely.	7288	6995
Nux Vomica	12	Alcohol.	5908	12	Hard.	6170	6055
Pareira Brava	60	Alcohol, 2 parts. Glycerin, 3 parts. Water, 5 parts.	7537	12	Moderately	8835	8020
Pilocarpus	20	Alcohol, 1 part. Water, 2 parts.	6943	16	Hard.	7698	7598
Pleurisy Root	20	Dil. Alcohol.	6727	14	Firmly.	7465	7278
Podophyllum	20	Alcohol.	5908	8	Hard.	6852	6290
Prickly Ash Bark, Northern	20	Dil. Alcohol.	6727	16	Hard.	7298	7149
Prickly Ash Bark, Southern	20	Dil. Alcohol.	6727	16	Hard.	7330	7120
Quassia	8	Alcohol, 1 part. Water, 2 parts.	6943	24	Hard.	7208	7115
Rhatany	20	Alcohol, 28 parts. Glycerin, 16 parts. Water, 21 parts.	7080	9	Loosely.	8390	8118
Rhubarb	20	Alcohol, 3 parts. Glycerin, 1 part.	6525	8	Firmly.	7785	7610
Sanguinaria	20	Dil. Alcohol, 86 parts. Acetic Acid, 1 part.	6824	8	Moderately	7780	7616
Sarsaparilla	6–30	Alcohol, 1 part. Glycerin, 1 part. Water, 3 parts.	7447	16	Moderately	7948	7800
Sarsaparilla Comp.	6–30	Alcohol, 1 part. Glycerin, 1 part. Water, 3 parts.	7447	18	Moderately	8045	7950
Scullcap	4–20	Dil. Alcohol.	6727	24	Hard.	7491	7290
Senega	20	Alcohol, 800 parts. Water of Amo. 5 parts Water, 400 parts.	6432	12	Firmly.	7630	7410
Senna	20	Dil. Alcohol.	6727	10	Firmly.	7816	7530
Senna Compound	20	Dil. Alcohol.	6727	16	Firmly.	7620	7512
Serpentaria	20	Dil. Alcohol.	6727	14	Hard.	7180	6963
Spigelia	20	Dil. Alcohol.	6727	14	Firmly.	7765	6510
Spigelia and Senna	20	Dil. Alcohol.	6727	16	Firmly.	7730	7540
Squill	entire	Dil. Alcohol.	6727	16	Loosely.	8898	8515
Stillingia	c.c.	Dil. Alcohol.	6727	16	Hard.	7153	7040
Stramonium Seed	20	Alcohol.	5908	8	Hard.	6188	6110
Uva Ursi	20	Alcohol, 2 parts. Glycerin, 3 parts. Water, 5 parts.	7537	8	Moderately	8856	8688
Valerian	20	Alcohol.	5908	8	Hard.	6248	6085
Veratrum Viride	20	Alcohol.	5908	10	Firmly.	6539	6390
Wild Cherry Bark	20	Alcohol, 7 parts. Glycerin, 11 parts. Water, 17 parts.	7554	12	Firmly.	8290	8113
Yellow Dock	20	Alcohol, 25 parts. Glycerin, 5 parts. Water, 70 parts.	7112	16	Firmly.	8122	7890

BROOKLYN, November 23d, 1878.

END OF REPRINT.

From 1878 to the present time 1887, the process of repercolation has been in continuous use as a manufacturing process under the writer's observation, upon all the principal drugs of the materia medica, and upon all quantities below 300 pounds at one operation, and many thousands of pounds of extracts and fluid extracts have been successfully made by it; and the progress made in working the process as described above may be briefly summed up, and brought to the present time.

The principal objection to the process has always been that a number of bottles,—generally about seven,—of weak percolates of varying strength, have to be carried and taken care of during the intermissions of the process, and this objection has neither been overcome nor modified to any useful extent, though a prolonged experience has shown that the disadvantage and inconvenience of this objectionable feature was much overrated. It is true that the weak percolates at the end of a series of repercolations may be evaporated so as to be either added to the finished preparation, or carried over in a single bottle; but either course interferes materially with both the present and future of the process, and the loss in quality of product and accuracy of process far overbalance the inconvenience of carrying the weak percolates separately.

The experience of the past five years has taught that many powders for percolation may be coarser than the sizes formerly given, and that all should be moistened with as much liquid as they will hold at the end of a maceration long enough to admit of a maximum degree of swelling of the powder, while leaving the moistened powder dry enough to be passed through a coarse sieve before packing. This management has such an influence both upon the rate and the extent of the exhaustion as to change the conclusions of the paper very materially. It is now found in practice to be quite easy to exhaust all the drugs very perfectly, and to easily make fluid extracts which fully represent their drugs in the proportion of minim for grain. A few hard and compact substances like some of the varieties of cinchona require to be in fine powder,—require long maceration and a much extended percolation for complete exhaustion, but then the result is easily attained and is fairly accurate. Few drugs, however well managed, are exhausted with less than 7 times their weight of weak percolate and new menstruum, while some require 10 or more times their weight. The relation of weight for weight is suggested and advocated in the paper, but as the number of drugs becomes larger, and the variety of menstrua greater,—and especially as the alcoholic strength of menstrua must vary from time to time, this advocacy is now considered to have been a mistake, and the older and now well established relation of minim for grain is considered much better, and quite unexceptionable.

This relation should never have been changed by the Pharmacopœia; and need not have been changed, for, if the present officinal formulas had directed that the 100 grams of substance should yield 95 cubic centimetres of fluid extract instead of 100, the old relation would have been retained. Upon these grounds a change to 95 c.c. is now advocated for the Revision of 1890. This is the equivalent of the older revisions of the Pharmacopœia, and the writer has never changed his practice from this.

During many years past almost all of the large manufacturers have claimed the adoption of repercolation for making fluid extracts, and since that the complaints of any heavy deposits occurring are chiefly confined to the products of the officinal process of evaporation by heating. With this there must always be deposits, but with repercolation there is practically no deposit other than that which occurs in winter from a summer-made fluid extract, because the menstrua saturated at summer temperature will not hold quite as much of the soluble matters at winter temperature. But as the menstrua are never saturated with the active principles of the drugs, it follows that these must be precipitated in very small proportion, if at all, by these changes of temperature: Fluid extracts should always stand about 3 to 4 months after being made before they are put up, and then, in the writer's experience in a 2½ gallon bottle, there is rarely more than half an inch of very light sediment which when filtered out amounts to but an ounce or two at most from 20 pints—generally not half that much.

In reviewing this part of the paper now, after an experience so much extended, it may be useful to emphasize by repetition the statement that with repercolation there is very little difficulty in making fluid extracts that fairly represent the drugs from which they are made, in the relation of minim for grain. Hence the quality of the fluid extract no longer depends much upon the process of extraction, but almost entirely upon the quality of the drug used; and the markets are quite as full as ever they were of poor drugs at low prices, the quality of which when made into extracts and fluid extracts is quite hidden from ordinary observation or testing. And yet good drugs were never more plentiful to those willing to pay the higher prices and apply the greater skill and care in selection.

The apparatus for repercolation is illustrated in the paper by four cuts, all upon the same general principle. The first and second cuts carry out the principles in one way,—the third and fourth in another. Both methods have maintained their utility by extended use in a great many different hands. The first two illustrated are the most simple and are perhaps best adapted to quantities of less than two pounds. Three percolators of ordinary form, arranged in one stand or group, and used upon this method, are illustrated in a new cut Fig. 7, upon this page. This group is the outcome of recent experience, and is very convenient for carrying on a con-

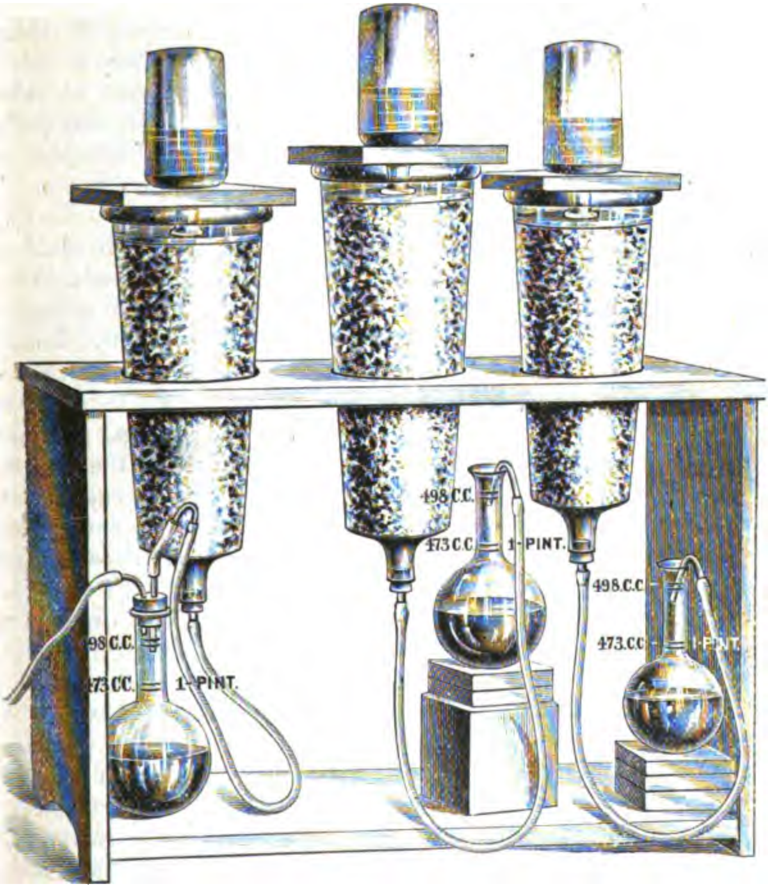
498 C.C.
473 C.C.
1-PINT.
498 C.C.
473 C.C.
1-PINT.
498 C.C.
473 C.C.
1-PINT.

Fig. 7.

tinuous series of repercolations wherein the weak percolates from one are passed on to the next, in due sequence and order. After what has been said of this method in the paper this new cut needs no description, except that on the left a provision is shown for the use of a Sprengel water pump or other form of aspirator, which is very convenient for hastening a percolation that is slow from accidental hard packing or other cause. The receiving flasks are so marked that they can be used for either one kilogramme of drug, equal to 15432 grains, to yield 498 c.c. of percolate at each measuring, or 15360 grains of drug to yield a pint at each measuring,—these being very convenient fractions for successful percolations of this quantity of drug. For farther illustration of this method by this apparatus, a table will be given farther on of a model series of repercolations of buckthorn.

The third and fourth illustrations of the reprint, where the percolate is drawn from within the percolator by an adjustable siphon, represent a method which more perfectly carries out the principle of having an equilibrium of downward motion of the liquid throughout the mass, and hence a more equable progressive exhaustion. The third cut Fig. 5, is a rather attractive and not inelegant piece of apparatus for the table of the practical pharmacist, and it is supposed to have had some influence in the desired direction of inducing the pharmacist to make his own extractions for extracts, fluid extracts and tinctures. The fourth cut Fig. 6, represents the form which prolonged experience has shown to be the best for large quantities. Stoneware pots of about six different sizes from 2 gallons to 100 gallons have long been in constant use in considerable numbers by the writer with great satisfaction and success.

The important table given at the end of the reprint, has, in the light of more recent experience, and from changes in the pharmacopœial strength,—or rather the pharmacopœial name, of alcohol and diluted alcohol,—been thoroughly revised, and brought down to the present time and practice, so that it is not reprinted, but has been rewritten with corrections and additions, and it is now therefore rather a part of this review than of the original paper, although left in its original position for continuity's sake.

FLUID EXTRACT AND EXTRACT OF BUCKTHORN.

It now only remains to give a practical illustration of the present condition of repercolation in the writer's hands, and for this illustration the important aperient Buckthorn, Alder Buckthorn, Rhamnus Frangula, or Frangula of the Pharmacopœia is selected, and the objects of the illustration are an extract and a fluid extract of the bark. The Pharmocopœia has a fluid extract, but no extract, and uses as a menstruum for exhaustion a mixture of one part alcohol and two parts water.

The buckthorn bark used in this country is all imported from Germany. In Germany the wood of the branches of buckthorn is used for making the charcoal for gunpowder, and has to be stripped of its bark for such use. The branches are easily peeled only during June and July when "the sap is flowing," and therefore it is that at this time all the bark is collected and dried rather as a collateral product of the making of gunpowder. These circumstances are of great advantage to the bark as a medicinal agent. First it insures the collection only of the bark of the branches, next it insures the collection and drying of the bark only at the proper season; and finally it renders it inexpensive and the supply sure, because the expenſe of collecting is largely paid in the value of the wood to the gunpowder maker. This uniformity of character, management and supply are most important to articles of the materia medica, because they almost insure the quality and uniformity of the articles.

After an investigation of the behavior of this bark with different menstrua some years before the last revision of the U. S. P. a menstruum of 4 parts alcohol to 15 parts water was adopted and recommended. But a short experience with this mixture upon a large scale led to an improvement by slightly increasing the proportion of alcohol to 25 p. c. and by adding 5 p. c. of glycerin. The mixture then consisted of 25 p.c. alcohol, 5 p.c. glycerin, and 70 p.c. water, and this has now been in successful use for the past eight years or more.

The chief advantages of it are, that the exhaustion is complete with the smallest practicable proportion of alcohol to yield a permanent finished product, and gives a fluid extract easily administered alone or diluted with water, wine or syrup to any desired degree, while the menstruum is an economical one yielding preparations of moderate cost.

The Pharmacopœia takes a No. 40 powder, and moistens this with 35 p. c. of its weight of the menstruum. The writer's practice is with a No. 20 powder, moistened with 75 p.c. of its weight of menstruum, when by a 24 hours' maceration before sifting, the bark is brought back to about its original condition of moisture in the fresh state, and has swelled to its maximum. It is then sifted and packed firmly, and allowed to percolate at the rate of about 60 drops per minute, when the quantity of dry powdered bark is 15360 grains (or a kilogramme = 15432 grains). And the fractions in which to receive the percolate on this scale of process, are very conveniently a pint, equal to 473 c. c. (or 498 c.c. if a kilogramme of powder be taken.)

The first pint of percolate from the first portion is reserved as finished, and the 2d pint and half of the 3d are taken to moisten the second portion of bark to be repercolated. This is macerated for 12 hours in a covered vessel, sifted and packed in the second percolator of the group, and then the fractions of weak percolate as they come off from the first portion are put upon the second until the first is exhausted. This exhaustion of the first portion is practically complete at the 8th or 9th pint for this scale of operation, but in this series of repercolations all were continued to the 15th pint, or about 7.5 times the weight of the bark. The last two pints may be safely pushed through by water without risk of getting water in the final weak percolates. The 1st and 2d pints from the 2d portion repercolated are reserved as finished, and are added to the 1st pint reserved from the 1st portion. The 3d and one-half of the 4th pints are used to moisten a 3d portion of bark which is macerated, sifted and packed in the third percolator of the group, as the others were, and the fractions of weak percolate from the second portion as they come off are put upon the third portion, each fraction being allowed to sink completely into the powder before the next one is put on. During the night or during the absence of the operator for any considerable length of time the percolations are stopped by blocking up the receiving bottles sufficiently high, or are made to proceed at so slow a rate as not to risk the surface of the powder becoming dry, or the overflowing of the receiving bottles. By a little care in adjusting the height of the bottle any desired rate of dropping may be established even down to 5 or 10 drops an hour, and when established it will go on with perfect security and regularity so long as the supply from the inverted bottle on top is kept constant. After the weak percolates from one portion are all put upon the next succeeding portion, from two to three pints of fresh menstruum are usually required before the water is used to push the last through. The 1st and 2d pints of percolate from the 3d portion of bark are reserved and added to the former reserved portions, and the 3d and half of the 4th pints are used to moisten a 4th portion of bark. By the time this is macerated the first percolator will have been exhausted. This is then carefully emptied without disturbing the disks of blanket and paper at the bottom, and then the 4th portion of bark is packed in the 1st percolator, and so the process is continued at will, and may proceed either interruptedly or continuously for years. The writer has processes under way, on various scales of quantity which have been practically unbroken, and rarely long interrupted for more than ten years, and the greatest advantage of this continuity of process is that the longer it is carried on the more accurately the reserved portion represents the drug in the desired proportion of minim for grain. This point is, however, reached with a sufficient degree of accuracy by the time the first four or five reserved portions are mixed. After that it only changes with differences in the quality of different parcels of the drug repercolated. The following table shows the results of a series of six repercolations of buckthorn. These results are presented with a good deal of detail, and will repay a careful examination by those specially interested in the process, but of course no such labor or detail is either necessary or useful in the actual practice of repercolation, but is only presented as an illustrative analysis of the process.

The table is divided into six subdivisions,—one for each portion,—and the subdivisions of the 1st and 6th portions are extended by three columns each to record the results of evaporations for the proportion of extract yielded by the fractions, thus showing the contrast between the 1st portion, which is a simple percolation, and the 6th, which is a repercolation.

The first column of the table gives the serial number of the fractions of a pint each, and applies to the entire six portions.

The second column gives the weight in grains of each fraction or pint of percolate from the 1st portion.

The third column gives the difference in weight in grains between the fractions of the percolate, and the same volume of the menstruum at about the same temperature. This indicates to a certain extent the rate and degree of absolute exhaustion, but the exhaustion of the medicinal parts precedes the absolute exhaustion by very much.

The fourth column gives the weight in grammes of 5 c. c. of percolate taken from each fraction, for evaporation in tared capsules.

REPERCOLATION OF BUCKTHORN BARK,—RHAMNUS FRANGULA.

The Bark was ground and passed through a sieve of 20 meshes to the linear inch, No. 20. The menstruum was 70 p.c. Water, 25 p.c. Alcohol and 5 p.c. Glycerin. Each portion was 15360 grains, or nearly 1000 grammes of the ground Bark, moistened with 1½ pints or 710 c.c., and percolated in fractions of one pint or 473 c.c. each. The column headed "Difference" is the difference in weight in grains between a pint or 473 c.c. of the percolate, and the same volume of the menstruum.

Pint or 473 c.c.	1st Portion.					2d Portion.		3d Portion.		4th Portion.		5th Portion.		6th Portion.				
	Weight of 1 Pint.	Difference.	Weight of 5 c.c.	Extract from 5 c.c.	Per cent. of Extract.	Weight of 1 Pint.	Difference.	Weight of 1 Pint.	Difference.	Weight of 1 Pint.	Difference.	Weight of 1 Pint.	Difference.	Weight of 1 Pint.	Difference.	Weight of 5 c.c.	Extract From 5 c.c.	Per cent. of Extract.
1st	7692	578	5.248	1.274	24.276	7841	727	7985	878	8017	905	7982	870	7941	829	5.423	1.625	29.965
2d	7584	470	5 181	1.066	20.575	7626	512	7766	654	7900	788	7747	635	7911	799	5.408	1.568	29.000
3d	7336	222	5.018	.647	12 893	7535	421	7594	482	7540	428	7595	483	7508	396	5.113	.842	16.468
4th	7211	97	4.930	.279	5.660	7390	276	7341	229	7285	173	7280	168	7242	130	4.965	.403	8.117
5th	7130	16	4.905	.183	3.731	7284	170	7238	126	7195	83	7197	85	7191	79	4.915	.321	6.531
6th	7128	14	4.920	.120	2.439	7261	147	7192	80	7172	60	7174	62	7168	56	4.905	.295	6.014
7th	7120	6	......	......	......	7206	92	7137	25	7159	47	7165	53	7167	55	4.903	.272	5.548
8th	7120	6	......	......	......	7214	100	7137	25	7150	38	7147	35	7158	46	4.885	.251	5.138
9th	7119	5	4.912	.056	1.546	7155	41	7130	18	7135	23	7140	28	7143	31	4.910	.235	4.776
10th	7128	14	4.920	.014	.284	7140	26	7126	14	7130	18	7135	23	7140	28	4.903	.191	3.895
11th	7120	6	4.911	.116	2.362	7125	11	7130	18	7132	20	7142	30	7142	30	4.891	.229	4.692
12th	7126	12	4.897	.106	2.163	7128	14	7121	9	7127	15	7137	25	7132	20	4.884	.174	3.562
13th	7128	14	4.904	.176	3.592	7129	15	7120	8	7120	8	7129	17	7125	13	4.869	.166	3.409
14th	7123	9	4.918	.038	.774	7120	6	7113	1	7120	8	7136	24	7119	7	4.890	.153	3.129
15th	7125	11	4.900	.080	1.633	7109	......	7120	8	7117	5	7129	17	7129	17	4.880	.170	3.483
Total	108190	1480	......	......	......	109263	2558	109250	2570	109299	2619	109235	2555	109216	2536	......	......	......
Menstruum	7114 at 25° C.	......	......	......	......	7114 at 25° C.	......	7112 at 25° C.	......	7112 at 25° C.	......	7112 at 25° C.	......	7112 at 25° C.	......	......	......	......

The 1st pint of the 1st portion, and two pints of each of the other portions=11 pints, were reserved and mixed as finished fluid extract, and 1 pint of this weighed 7910 grains.

The 5 c.c. of this finished fluid extract weighed 5.358 grammes, and gave 1.588 grammes of extract, or 29.64 p. c.

The 5 c.c. of the menstruum weighed 4.898 grammes, and gave .245 grammes of extract, or 5.000 p.c. of glycerin residue that would not evaporate off under the conditions adopted in all the evaporations for percentage of extract.

The capsules and contents were placed in a steam oven and dried until they ceased to lose weight.

The fifth column gives the weight in grammes of this dried extract. The 5 c.c. from the 10th pint of the 1st portion was the last, which gave a solid or semi-solid extract. All after that were liquid, and to the touch and taste seemed to be only dilute colored glycerin.

The sixth column gives the percentage of the extract obtained from the different fractions of the 1st portion. At the foot of the table will be found a record of the weight of 5 c.c. of the menstruum. This being evaporated under the same conditions as the weak percolates were, the weight of that portion which did not go off by evaporation, is given and the percentage. But if this percentage be accepted as a constant quantity to be subtracted from all the percentages of the column, it will be found not to apply below the 4th pint or fraction. This shows that more glycerin evaporated off from the weak percolates than from the menstruum under the same conditions.

The seventh and eighth columns give the weight and difference for the fractions of the 2d portion of bark.

The ninth and tenth columns give the same results for the fractions of the 3d portion of bark.

The eleventh and twelfth, and the thirteenth and fourteenth give the same results for the 4th and 5th portions of bark.

The fifteenth, sixteenth, seventeenth, eighteenth and nineteenth columns give for the 6th portion the same details that the corresponding columns for the first portion do, and show the strong contrasts between these first and last portions of the series. If the percentage of residue from the evaporation of the menstruum be applied to the last column, it will be seen to become inapplicable below the 8th pint or fraction, and all the extracts below this point were liquid, whilst the 7th and 8th were nearly liquid.

These results clearly indicate,—and the indication was confirmed in practice on the large scale,—that in making the solid extract it does not do to evaporate down all the weak percolate, because this yields an extract which cannot be brought to a pilular consistence by evaporation. In practice the first two fractions only should be taken for extract, the others being carried onward for repercolation of fresh portions of bark. These, however, yield an excellent extract, which can be easily evaporated to a pilular consistence with a low degree of heat. That is, the fluid extract should be taken for making the solid extract, and when this is evaporated until the extract weighs about 30 p. c. of the bark represented it will be of a good pilular consistence, and will represent the bark in the proportion of about 1 grain to 3¼ grains of the bark, and will represent the Fluid Extract in the proportion of 1 grain to 3¼ minims.

At the foot of the table, below the line of totals, is given the weight of 1 pint of the menstruum weighed at 25° C. or 77° F., which was about the average temperature at which the percolations were made. This taken as a constant weight and subtracted from the weight of the same volume of each fraction, gives all the six columns of differences.

This drug and its preparations have been generally underrated in value by the best authorities in common use in this country, and it has taken it about 15 years to live down the equivocal character generally given to it. Writing from memory, and therefore rather indefinitely, the writer does not remember it among the used articles of the materia medica of this country until about 15 years ago, when the late Dr. John P. Gray of Utica returned from a visit to continental Europe with a bag of buckthorn bark, and a knowledge of how to use it. Gentle aperient medicines are especially valued in the treatment of the insane, and this with Dr. Gray's knowledge and example soon taught others how to use buckthorn bark, and induced the writer to make the first importations of it in any considerable quantities that are known to have come to this country. Up to this time Dr. Gray had used it and advocated its use in substance, and there is probably now no nicer or better way of using it than by chewing small fragments of the bark two or three times a day for two or three days, or until a gentle aperient effect is obtained. But insane patients could not be well treated in this way, and decoctions and infusions of the bark were not permanent, and were bulky and inconvenient. A fluid extract, suggested by the writer, was found much more convenient, and very easily managed in regard to dosage and administration. And from that time (1871) to this,—without a line of advertising in any shape, it has grown into a very considerable usage all over the country, and it has now so far overcome the indifferent reputation given it by the best authorities, that it is rather strange they do not review the subject and rewrite their paragraphs of its medical properties and uses. In order to be the drastic cathartic as so often described, with its train of disagreeable effects such as nausea, vomiting, violent purging, etc., it must be taken in the fresh condition, in which it is never accessible here, or must be taken in quantities so irrational that it never is so taken. It has properly been admitted to the last revision of the Pharmacopœia, and the direction is there given that it should be collected at least a year before it is used. This direction is not found in the German Pharmacopœia, where the bark has been longest officinal, but is found in the last British Pharmacopœia, where it is officinal for the first time. It is well known and often stated that the fresh bark is more active and more irritant than the dried bark, and it is supposed that the older the better.

In its action upon the intestinal canal buckthorn and its preparations resemble those of rhubarb and senna when these are of the best quality, but is much milder and more managable than even the best senna, and rather more agreeable in effect than rhubarb, and applicable to a different class of cases and uses.

In properly adjusted doses,—that is, doses not too large,—it is perhaps the mildest and simplest of all aperient or laxative medicines, and the easiest to adjust to a desired effect. Its operation is slow, but fairly certain, and its action continues throughout the whole tract. Rhubarb and senna affect chiefly the upper part of the tract, and have to be given in almost purgative quantities to affect the whole tract. When a mild purgative or evacuant is wanted, rhubarb and senna are better; but when a mild aperient or laxative, for delicate organisms, is wanted, buckthorn is better. When a mild degree of constipation is to be corrected without exciting reaction and without requiring continuous medication the buckthorn is much better, and when used with skill it seems to leave little to be desired. The dosage of buckthorn is a most important element in its proper use, and the different impressibility of different individuals to its influence makes this dosage the chief difficulty in its appropriate use. Bearing in mind that it is a simple aperient, (*ab and pario,*—'I bring forth;' 'I open.'—Dunglison) and one slow in operation, those who use it will easily guard against giving it in too large quantities, or expecting a too prompt response to its use. Where either a very decided or very prompt response is needed other agents are better. The limit of its use in this direction seems to be a fluidrachm of the Fluid Extract at bed-time where a temporary costiveness,—not constipation,—is to be relieved during the forepart of the following day. When temporary costiveness has passed into habitual constipation, 20 minims in a little water one, two or three times a day is a better dosage, with the expectation of a partial improvement on the second or third day, when the number of doses are to be diminished. With a numerous class of delicate and sensitive women such a treatment will be generally successful, the management being easily varied to suit the conditions. Adult men, of inferior impressibility will, of course, require larger quantities, but the character, and the appropriate uses of the agent will always limit the dose to about one or two fluidrachms, and make it better to repeat the doses than increase the quantity at one dose.

Many physicians use the Fluid Extract as an evacuant, but with doubtful propriety when castor oil, rhubarb, senna, and the compound cathartic pill are so much better. But as a mild aperient to overcome either temporary or habitual constipation buckthorn is hardly equalled in the materia medica.

The extract is given in pill or capsule, and 4 to 5 grains is generally an effective dose if given at bed-time for two or three days; —5 grains being the equivalent of about 16¼ grains of the bark, or 16¼ minims of the Fluid Extract.

Of the Fluid Extract 15, 20, or 30 minims, according to circumstances, if repeated at bed-time for a few days will be effective in a large class of cases where there is no urgency.

The taste is very mild, sweetish bitter, recalling that of a mixture of liquorice and wild cherry bark. It is not disagreeable to most persons, and is rather agreeable to some, and it is therefore not difficult to administer even to children. While rarely offending the palate, it never offends the stomach, and as a rule requires no corrigents, and is not improved by combination with other agents. The Fluid Extract, diluted simply with half a fluidounce of water at the time of taking each dose, makes a muddy looking liquid, but is very easily taken, and this is perhaps the best way to administer it. But if diluted with a mixture of equal measures of diluted alcohol, or brandy and syrup, so that each dose may be 1 or 2 fluidrachms of the dilution, it makes a very clear, elegant preparation of a rich, dark color and agreeable taste.

The British Pharmacopœia (1885) gives the dose of its Extract as 15 to 60 grains. Its Liquid Extract is made by the objectionable method of boiling the bark four times with water. When finished it bears the same proportion to the bark as the U. S. P. Fluid Extract, but contains a little less alcohol. The dose given is "1 to 4 drachms." These doses for both Extract and Liquid Extract, if they represent British usage, are so large as to indicate that it is used as an evacuant or purgative, and therefore that its individual or characteristic effect or advantage in small doses as an aperient, is missed.

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VOL. III. No. 3.

AN
EPHEMERIS
OF
MATERIA MEDICA, PHARMACY,
THERAPEUTICS
AND
COLLATERAL INFORMATION.

JUNE, 1888.

BY
EDWARD R. SQUIBB, M. D.
EDWARD H. SQUIBB, S. B., M. D.
CHARLES F. SQUIBB, A. B.

BROOKLYN, N. Y.
1888.

NOTICE.

A list is kept with care of all who are supposed to be specially interested in Materia Medica and Pharmacy, and however irregularly and infrequently these pamphlets are published, one copy of each issue is mailed without charge to each name on the list, and the list is, as it always has been, freely open to new names that may desire to be upon it.

But after an issue has been distributed, neither copies of that nor any other back issue can be sent free of cost, and all orders, to receive any attention, must be accompanied by ten cents in postage stamps or postal note for each pamphlet wanted.

The two completed volumes, separately bound in cloth, are still accessible to any who may want them and will remit $1.16 for each or for either volume. On receipt of the money they will be mailed postage paid.

AN EPHEMERIS

OF

MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

VOL. III. JUNE, 1888. No. 3.

The following errors in the last Ephemeris have been discovered:

On p. 988, in the account of the cost of manufacturing cocaine, the "estimated rent" is carried out at $34.00. This was calculated for one month, and the multiplication by ten was omitted. It should have been $340.00.

In the two items next following, exactly the same blunder was made, and they should stand,—instead of $27.00, $270.00, and instead of $20.00, $200.00. These errors add $729.00 to the footing, and make it $4,479.00, instead of $3,750.00.

It is necessary to correct these mistakes if the details given be used to ascertain or justify future estimates of cost, because these will be stated in a different way,—namely, at so much per pound of cocoa.

At p. 1044 a foot note was accidentally dropped out of a large proportion of the pamphlets printed.

This foot note is needed to make the preceding cut clear, and the asterisk referring to it should be at the "498 c.c.," ninth line from the top of the page.

The foot note is as follows:

This 498 c.c.—or more literally, 500 c.c.—gives the U. S. P. relation of about .95 grain of the drug to each minim. If the older and better relation of 1 grain in each minim be desired, then about 475 c.c.—or say 1 pint and 33 minims should be the measure of the fraction.

APERIENTS.

By Edward R. Squibb, M. D.*

The Executive Committee has appointed this evening for the discussion of the every-day subject of aperients, to the end that by an interchange of knowledge and experience all may be benefited in relieving and preventing the conditions to the correction of which aperients are applied.

At the outset of such a discussion it may be well to try to get definite ideas,—first of the conditions to be relieved; and next of the means and agents for relieving those conditions.

The principal condition is universally known as constipation. The word constipate is defined by Richardson—"To compress, to condense, to thicken, to cram or squeeze close, to close up or stop up," and this definition gives a very clear idea of the condition. But it is necessary to go farther than this, because the causes of the condition are of an importance at least equal to the condition itself. A cathartic will promptly open or unstop that which was closed up, but will commonly leave the cause of the condition unchanged, and therefore liable to recur as promptly as it was relieved. The causes of constipation are doubtless neither simple nor single but always complex, yet it may aid in a practical consideration of them for the purpose at present in hand, to single out two of the most common proximate causes, and consider them as though acting separately. Food and drink as taken into the stomach are naturally in the condition of a thick fluid mixture, and the nutritive portions are absorbed out from the residues in a solution fluid enough to be carried and distributed to all the tissues of the organism. When fluid enough is taken up to hold the nutritive matters in solution and to supply the circulatory system, the residuary matters are naturally left with enough liquid to render them pultaceous and keep them so. Then the secretions from the mucous linings of the canal, for lubrication, and the peristalsis for progression, are the natural means whereby they are carried through the intestinal tube and finally voided in the natural soft solid condition, and there is no constipation. But if there should be an unusual loss of water by cutaneous or pulmonary transpiration, or by active diuresis, the deficiency will be supplied as far as possible from the food residues by increased absorption, so that by the time these residues reach the colon they will be so compressed, condensed, thickened and squeezed close, as to constitute constipation, with deficient liquid ingesta, or excessive liquid excretion by skin or kidneys, or both, as prime causes. As in the normal condition the contents of the intestinal canal are found to increase gradually in consistence from the pylorus to the rectum, being fluid above and soft solid below, it follows that the absorption of moisture from the residues must be a continuous process throughout the whole length of the tract. And from this it again follows that the more rapidily the contents are carried along the tube the less time will there be for the abstraction of the water that gives them fluidity and mobility; and this introduces the second prime cause of constipation, namely, slow or defective peristaltic action.

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* Read before The Kings County Medical Association, October 4th, 1887.

The vermicular contractions and dilatations which push the contents of the tube from the pylorus to the rectum may be excessive or defective in force or in frequency, or in both, to any degree from abnormal activity as in diarrheas, or in the action of cathartics, to the abnormal inactivity of obstinate constipation,—or obstipation. When defective, and the rate of absorption of the watery part which gives fluidity and mobility is continuous, the excretions may become so inspissated and contracted in volume in the colon as to be too small to be effectively grasped and propelled by its slow and defective contractions, and so solid as to easily fall into its pouches and lie there almost indefinitely or until they accumulate to a volume which is large enough to be feebly grasped by its defective contractions. Then, next follows impaction in the rectum,—the last stage of constipation, and anything may, of course, constipate any individual which brings these causes into active operation either slowly or rapidly. If slowly, then there is the constipated habit, and the time necessary for any agency to overcome it. If rapidly it is generally the result of easily recognizable changes of diet, or clothing or exercise.

After such a brief definition of constipation in relation to some of its principal causes, what is an aperient?

In ordinary parlance, as well as in the literature of the profession, there are cathartics, purgatives, laxatives and aperients, and these terms are frequently used as being practically synonymous. That they have really, and should have a different significance will hardly be questioned. Cathartics and purgatives are nearly allied, and so are laxatives and aperients, but the difference between a purgative and a laxative is great, and between a cathartic and an aperient greater.

In order to realize these differences and apply them practically it may be useful to review the derivations and definitions of the words as given by good authorities.

Richardson gives the Greek derivation of cathartic and translates it as "purifying or purging, cleansing," and quotes Plato as saying that mathematical demonstrations are the "cathartics or purgatives of the soul, as being the most proper means to cleanse it from error, and give it a relish of truth." Modern usage, however, has changed or extended this definition, and differentiated cathartics from purgatives. Cathartics are not only cleansing evacuants, but are revulsive and depletive, and some of their best offices are as counter-irritants. They increase the peristaltic force and frequency, and thus hurry the ingesta through the canal in a liquid state, and at the same time so excite the mucous linings as to cause the excretion of water or serum from the blood and thus become actively depletive. By their activity they are revulsive and counter-irritant, greatly relieving any local or general tension in the organism by an irritation which is transitory and self-limiting. As they leave a condition which highly favors constipation they are not appropriate to its treatment, but are commonly well applied only to a very different class of cases.

The word purge is from the same derivation as pure, which means "cleansed or cleared by fire" (Richardson), and hence purgatory as another word from the same Greek root.

To purge is "to cleanse, to clear, to scour, to wipe off, to clear away, to eject or expel foulness or filthiness, physical or moral; to clear from accusation, to excuse." (Richardson.) This author gives many illustrations of the older meanings of the word. Among them from Quintüs Curtius: "Thereupon they fell to weeping and purging of themselves," and from Bacon: "Surfeits many times turn to purges both upwards and downwards."

Falstaff well illustrates the older meaning when he promises to "purge and live clean like a gentleman."

The best modern medical usage, however, seems to restrict the use of a purge to the simple evacuation of the canal whether to carry off irritant matters, or simply to empty and cleanse the tract without much revulsion or depletion or counter-irritation, and therefore without the reaction and prostration which follow catharsis. It is easy to purge by moderate or small doses of cathartics, and to produce catharsis by large doses of purgatives, and so far the words only signify different degrees of the same action, but yet it is highly conducive to that precision of language aimed at by modern medical science to use different words only when there is a difference in meaning. Dunglison (Medical Dictionary) makes cathartic and purgative almost, but not entirely synonymous; but since his time the drift of careful writers and close observers has been to draw a practical distinction between them. If many writers still confuse cathartic and purgative action, there are few who do not distinguish between these and laxative or aperient effects.

Richardson derives lax and laxative from the Latin laxare, to loose, and in this sense of lax,—loose,—it means "slack, untied, unfastened, unconstrained, unrestricted, dissolute." Dunglison, (Medical Dictionary), defines a laxative as a "medicine which gently opens the bowels; such as tamarinds, manna," etc., and the same authority defines an aperient also "as a medicine which gently opens the bowels. The term formerly had a much more extensive signification, and like catalyticum, was given to a substance supposed to have the power of opening any of the passages, and even the blood vessels," making it synonymous with laxative. Richardson derives aperient from "apert,—Latin apertus, the past participle of aperire (ad parere, to bear), to bring before, or into public view. Brought into public view, open, uncovered, undisguised, unconcealed."

Dunglison derives it from ab and pario, "I bring forth," "I open." To loosen and relax, and to bring forth and to open, are therefore seen to be but different modes of expressing the same effect.

But modern good usage seems to be gradually tending to make a distinction in the direction of useful precision, which distinction is based less upon difference in effect than upon a difference in the class of agents used to obtain the effects.

It is said that rye, oatmeal, bran bread, honey, and fruit in general, especially figs, prunes, dates, tamarinds, etc., are laxative in effect, and therefore laxatives, though hardly medicines in the common acceptation of the term. Aperient medicines are quite numerous, but always medicines. Laxative medicines are also heard of, but perhaps less frequently than laxative foods, and certainly less frequently than aperient medicines.

Aperients therefore are medicines,—not foods,—which gently open the bowels, and thus oppose and correct constipation by producing a laxative effect. Unlike cathartics they are slow and mild in action, yielding neither revulsive nor depletive effects, nor any degree of prostration.

Unlike purgatives they do not empty and cleanse out the alimentary canal, but simply prevent the desiccation and condensation of the excreta so that they do not close up or stop up the lower passages, and they do this either by preventing the undue absorption of the diluting and thinning liquids of the canal, or by gently stimulating the force and frequency of the natural peristaltic action so that the excreta are pushed along to the exit before they have time to become inspissated and unmanageable through perverted action or inaction.

When the agents used are considered, the distinction between the sections of this group of effects is emphasized. Colocynth, colchicum, croton oil, elaterium, jalap, scammony, podophyllum resin and the sulphates of magnesium and sodium are cathartics, and no one would think of using them as aperients, though in small quantity any of them might enter into aperient combinations.

Then butternut, castor oil, rhubarb, senna and many salines are purgatives or evacuants, and either simply, or variously combined, they clear out the intestinal tract. These much more frequently enter into aperient combinations than the cathartics, but in their initial capacity or quality they are purgatives. The distinguishing characteristics of aperients is their appropriateness to gently stimulate all the functions of the alimentary canal. By improving the condition of all the coats they improve digestion and absorption and promote secretion and excretion, and thus favor both alimentation and nutrition sometimes to the extent of revolutionizing both the physical and moral conditions of the sensitive, semi-invalid class, whose modes of living make the individuals so liable to constipation. In this they are widely distinguished from cathartics and purgatives. These latter empty the canal, and an empty canal is abnormal. Aperients do not empty the canal, but stimulate it to increased activity and relieve or unload it gradually without emptying. It is true that the careful skillful use of cathartics and purgatives, may do this, but then they are no longer cathartics and purgatives, but become aperients.

The very common need and utility of aperients through so many generations, and the different impressibility of different individuals to any single aperient medicine, has so multiplied these agents that there is a very large number from which to select; and their skillful use often depends largely upon this selection, and the changing from one to another until each individual case is suited.

From what has been said of the nature and causes of constipation it will be seen that modifications of diet will often give the desired aperient effect; especially when these modifications are in the direction of more succulent food, or the larger use of water either with food or in the intervals between meals.

Three or four glasses of water more than is customary in each 24 hours for a few weeks will occasionally correct habits of constipation; and will generally aid in the correction when insufficient if used alone. And if the water thus used should hold a small proportion of salines to give it the character and name of a well advertised mineral water, so much the better. Many of the mineral waters, artificial as well as natural, through the character and quantity of the salts they hold, as well as by the water of dilution, are very efficient aperients, but with the frequent disadvantage that when discontinued the constipation is liable to recur. This disadvantage is common to the use of all salines as aperients, and may be partly overcome by the use of simple water after the discontinuance of the salines. The different aperient effects of different mineral waters on different persons, and on different conditions in the same person, are well known, so that here as with more active aperients there is much need of skill in making selections.

From some simple proceeding, by diet or drink, to the most complex prescription, the physician can select from a very large number of aperients and can try one after another until his individual cases are best suited.

The Pharmacopœia offers many excellent aperients in various eligible forms, and it is doubtful whether, in selecting, there is ever need to go beyond its limits.

One admirable feature noticeable in almost all the officinal aperients is that they are especially addressed to the lower large intestine, where impaction and all the worst effects of constipation are to be met, by containing aloes of the best variety.

The officinal Confection of Senna, Compound Fluid Extract of Senna, Mixture of Rhubarb and Soda, Pills of Aloes, Pills of Aloes and Asafœtida, of Aloes and Mastic, of Aloes and Myrrh, the Compound Pills of Rhubarb, and the Compound Effervescing Powder, are all prominent and excellent aperients when doses are carefully adjusted to individual cases as they arise. But for general use perhaps none of these excel the simple fluid extract of buckthorn bark, which the Pharmacopœia calls "Fluid Extract of Frangula."

The Confection of Senna, which consists of 10 p.c. of its weight of finely powdered Senna (Alexandria), in a confection of the pulps of purging cassia, tamarinds, prunes and figs, guarded in its tendency to gripe by the effective corrigent coriander, is a most excellent aperient, especially adapted to those cases in which the sluggish action is prominently in the small intestine. A patient may be supplied with a quarter or half-pound jar of this Confection and be directed to take out with a scissor-blade a portion varying in size from that of a pea to that of a marble, according to the effect of the first doses taken. The portion is rolled into a bolus between the thumb and fingers and swallowed at bedtime, or oftener if this be not sufficient.

A useful modification of this kind of aperient, of milder or stronger effect, is made by taking a jar of French prunes, incising each one and removing the stone. They are then counted and an intimate mixture is made of two or three grains of Aromatic Powder, or as many minims of fluid extract of Aromatic Powder, and one or two or more grains of Senna, or Rhubarb, or Buckthorn, or Cascara, or Aloes, or indeed any desired aperient, to each one of the number of the prunes. The mixture is divided then by the number of prunes, and the proper portion is then put into each prune, and each is pressed firmly upon its contents, which have taken the place of the stones. They are then repacked in the jar, and in 24 hours are ready for use, but are better after standing for a week or two. These may often be given to very sensitive women and children who resist taking medicine in any more disagreeable form. And one or two of such prunes daily may be made so as to have a good aperient effect without being disagreeable when eaten.

The officinal Resin of Podophyllum is a harsh and drastic agent when used in even moderate doses alone, but in small doses well diluted and well guarded, and not repeated too frequently, it is a most efficient aperient. Its characteristic qualities are that its chief action is upon the upper part of the small intestine, stimulating the liver or overcoming atony, in the same way that mercurials do. In operation it is very slow but very sure, and its slowness often tempts physicians not accustomed to its use to a too frequent repetition.

In 1866 the writer proposed a compound pill of resin of podophyllum for especial use as an aperient in cases where the upper part of the alimentary tract was most in fault, perhaps through sluggish action of the liver. These pills were found so useful that two years later in January, 1868, the formula was published in The American Journal of Pharmacy, Vol. XL., or New Series, Vol. XVI., p. 11, and for the past twenty years they have been largely and effectively used, being commonly known as "Podophyllum Pills" or "May-Apple Pills." Each pill contains a quarter of a grain of Resin of Podophyllum, and either one grain of Alcholic Extract of Hyoscyamus, or an eighth of a grain of Alcoholic Extract of Belladonna, and one grain of powdered Capsicum, with one grain of powdered sugar of milk and a quarter of a grain of powdered acacia, as diluents. These are very thoroughly mixed so as very thoroughly to divide and dilute the resin, and then about one-third of a grain of glycerin is added to keep the pills soft and surely soluble in the stomach. The pilular mass is then made up with syrup and very thoroughly beaten. Nowhere is the knowledge and skill of the expert pharmacist so necessary as in making such pills, and a pill to be surely soluble in the stomach, and to be effective there and in the duodenum, by actual contact of its ingredients, should surely never be coated.

To act as aperients in overcoming habits of constipation, these pills should be given at bedtime, and very rarely more than one at a time. No effect need be expected on the day following, but the second or third pill at bedtime will pretty surely give some effect on the third or fourth day. Then, usually, one dose at bedtime is to be omitted, and by the end of a week two doses a week will be sufficient during the next week, one dose a week for the third week, and finally none.

The simplest and least disagreeable of all the aperients and perhaps the one to which the most fastidious persons least object is the Fluid Extract of Buckthorn, or Frangula, as it is badly named by the Pharmacopœia. This makes a clear solution with any proportion of the officinal Diluted Alcohol or with brandy, or may be more usefully taken in the less sightly dilution with water.

The main difficulty with this aperient is the adjustment of dose to different individuals. When given in just the right quantity the individual is rarely sensible of any effect excepting the desired aperient effect, and in some persons 10 minims will give this effect, while in others a fluidrachm may be too little.

In a typical case of habitual constipation wherein the morning evacuation had to be patiently solicited for ten minutes to a quarter of an hour, with the general result of a small scybalous mass, but with occasional disappointment, twenty minims of the Fluid Extract in half a fluidounce of water taken at bedtime would have no effect on the next morning's dejection. But about midday or later,—say from 14 to 18 hours after taking, there would be a call,—not very urgent, but not to be resisted very long, with the result of a fairly copious natural dejection. The following morning a smaller one of similar quality, and then for two or three mornings more, fairly natural dejecta, but approaching the old condition sufficiently to suggest a repetition of the dose. But, two doses a week for three weeks, and then one dose a week for three weeks more, corrected the habit permanently without change in diet or drink.

The dose is not very disagreeable to most persons, the taste feebly recalling that of a mixture of liquorice and wild-cherry, but without the sweetness of the first and with less bitterness than the second.

A fluid extract of cascara made exactly parallel to that of buckthorn, given in the same quantity to the same person, had the same general effect as the buckthorn, but operated less pleasantly. When the two were alternated many times at intervals of about a week, a decided difference in favor of the buckthorn was observed. The call on the day following the dose of cascara occurred about the same time, but was attended by a slight degree of discomfort and after-straining,—a sense of unfinished operation,—from which the buckthorn was free. The character of the discharges was apparently the same from both, and was entirely normal in color and slightly less than normal in consistence, and neither agent lost any power by frequent repetition, but both rather gained, if there was any change in activity. The cascara was by far the most disagreeable dose,—much more bitter and less aromatic, and so persistent was the bitterness that it was present in the mouth on the morning following the dose.

Quite enough has now been offered to elicit the views and the experience of those present, whether members of the Association or not, on this very common subject. And as all are able to speak on such subjects, it is hoped that the interchange of views will be general.

The foregoing paper was read at the stated meeting of The Kings County Medical Association, held October 4, 1887, to open the subject which had been appointed for that meeting. The discussion brought out much valuable experience, and those present were glad to compare and improve the methods they had fallen into of relieving the common disorder of constipation. Among the points made during the discussion, two important ones were brought out.

It was shown that in many cases of constipation where the sluggish action of the canal resulted from depressed conditions of the nervous centres, it was useful to add a small proportion of extract or fluid extract of nux vomica to the aperient used. Without this addition in such cases, the relief was often temporary.

The other important point was that the administration of the aperient should be so timed as to produce its effect at the habitual hour for the daily evacuation. For example, the best and the common time for the daily habit was after breakfast in the morning. If the aperient when given at bedtime was without effect at the usual time, but did operate two or three hours later, it was best to give it two or three hours before bedtime, so as to obtain its effect at the habitual hour and thus confirm the habit.

NOTE ON ANTIPYRETICS.

By Edward R. Squibb, M. D.[*]

The word "antipyretic," although not new, has but recently come into common use as a substitute for the word "febrifuge." The words are synonymous and of the same ultimate derivation. Antipyretic is that which is opposed to fire, and fever comes from fire. Febrifuge is that which causes fever to fly, or to be fugitive. Hence the significance of both words is to oppose, counteract or dispel fever. The choice between the words seems to be a matter of taste or fashion, and febrifuge seems to be going out of use.

The oldest and best febrifuge is quinine, and this still stands at the head of the class of newer antipyretics. The origin and application of quinine are too well known to require notice here, and its value is too well established to be in much danger from the more modern agents. Until quite recently the great drawback to the use of quinine was its high cost, and almost all the recent antipyretics were discovered through the efforts of chemists either to make quinine artificially, or to make substitutes for it. The making of quinine synthetically or artificially, although several times announced, has not yet been accomplished; and its great abundance and low cost for the present, and probably also for the future, have taken away the incentive to make it synthetically, because if so made it could not be so very much cheaper than from natural sources; and therefore it does not offer the inducement of the very large profits offered when the natural product was so costly. But the modern research in this direction has yielded very interesting and important results, in addition to the still increasing list of substitutes or antipyretics.

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[*] Read before The Kings County Medical Association, November 1, 1887.

A brief notice of only the more prominent substances of this list is all that can be undertaken here, and all the material for this is compiled from a few of the numerons authorities on the subject. Nothing original is offered, and nothing as being very accurate, because every article of the list is put forth with the conflicting statements so apt to result from the combined influences of pecuniary interests, enthusiasm, and limited observation stimulated by the universal appetite for novelties.

CHINOLINE.

In 1842 Gerhardt, by distilling quinine with caustic potassa and water, discovered a base which he called quinoline, but the dearness of quinine forbade attempts to utilize the base from that source. By treating cinchonine in the same way he obtained another base which he named chinoline, and the comparative cheapness of cinchonine encouraged the investigation of chinoline and its salts. These were found to be active antipyretics, and the base was used through many years as a nucleus from which various chemical substances were built up of varying character and power as antipyretics or quinine substitutes.

In 1880 Dr. W. Königs, of Munich, gave a new impetus to the researches based upon chinoline, by making this in quantity synthetically or artificially from aniline. He was soon joined by Baeyer, Skraup and others in a new order of investigations, which have been very fruitful, and are still in active progress.

The tartrate of chinoline was one of the earliest antipyretics, and was largely used. It is still in the markets, and still occasionally used, but has given place to more recent agents.

RESOIN OR RESORCIN.

About 1862. Hlasiwetz and Barth, following up Gerhardt's idea of 1842, distilled certain resins with alkalies and water, and obtained a substance which they called resorcin, because it was obtained from resin and was similar to orcin from archil or orchil. Subsequently Korner prepared resorcin synthetically by building it up from a benzol nucleus, and from its constitution it is meta-dihydroxylbenzol and belongs to the phenols.

Like salicylic acid it was first used and extolled as an antiseptic, and it was brought into prominence chiefly by Dr. Justus Andeer, of Wurzburg. Later, in 1880, Dr. Lichtheim, of Berne, showed that it was also an active antipyretic, with many effects analagous to salicylic acid, and for some time it was used quite largely.

SALICYLIC ACID.

Salicylic acid had been long known and many of its characteristics well studied, when in 1874 investigation into its therapeutic effects and use gradually led up to its antipyretic action now so well known, but with insufficient investigation it has had to give way to agents with newer claims.

KAIRIN, OR KAIRINE, AND KAIROLINE.

In 1882, the investigations of Drs. O. Fischer and W. Kōnigs, of Munich, on the alkaloids, assumed that the characteristic properties of quinine were not based upon the chinoline nucleus, but by the introduction into this nucleus of an oxygen bearing or a hydrogen bearing element. A number of substances were prepared in following up this new departure, and these were submitted for physiological investigation to Dr. W. Filehne, of Erlangen. The net result of these joint labors was the production by Dr. Fischer of oxychinolinmethylhydride which was called kairine, and by Dr. Kōnigs, of chinolinmethylhydride, which was named kairoline. The first of these soon after became the kairin of commerce, and having been patented, was extolled and advertised into a large usage. This seems to have been the first of the antipyretics that was started as such, and it was more largely used for a time than any of its predecessors; and it did more to introduce the fashion upon which its successors were to be still more largely used. It was the first one to be stimulated by the mercantile influence of a patent, and the patentees took good care that all that could be said in its favor should be widely advertised. Therefore it was very largely sold and used, and laid a good foundation for its successors, as its disadvantages were slowly recognized. The patentees are also the patentees of its immediate successor, antipyrin, and they are the well known enterprising color makers, Meister, Lucius and Brüning, of Hoechst, Germany. Each package of kairin is labelled as being protected by letters patent in Germany and the United States, and importation into France prohibited.

ANTIPYRIN.

In the early part of 1884, Dr. L. Knorr, of Erlangen, synthetically prepared an oxygenated alkaloid which he called antipyrin. This was investigated therapeutically by Prof. Filehne, who reported that it was an active antipyretic. For some months nothing was published in regard to the character or composition of this substance, but when it had been patented and introduced into commerce by the color makers above mentioned, Dr. Knorr published a paper stating that antipyrin was a derivative of an hypothetical base which he called chinizin, the systematic name being dimethyloxychinizin. Its antipyretic action was soon reported upon very favorably by many German observers of note, and it was made on a large scale and well advertised at a high price, but not so high as kairin. As it came into use the makers sought to patent it in other countries, and found no difficulty in extending the German patent to the United States. But in France there was difficulty. In the political economy of France, and to the great honor of the nation, it has long been held that the interests of suffering humanity are superior to the interests of inventors, and therefore, as a sanitary measure, patents upon medicines are not granted, and patented medicines from all sources are prohibited. The German patentees were part owners in a color-making company in France, and through this connection obtained a patent on the process for manufacturing dimethyloxychinizin as an aniline product. But as it was not used for any industrial purposes, and could not be sold as a patent medicine, the French patent could not be used; and as processes and articles patented in France but made elsewhere are absolutely prohibited, France seemed to be excluded from the use of antipyrin as well as kairin, unless it be admitted that any chemical manufacturer or pharmacist in France has the legal right to make and sell such articles when used only as medicines, without regard to the patent rights of other nations. This point is understood to be still unsettled, and every parcel of kairin and antipyrin bears on the label, "Importation into France prohibited on account of the French Patent Laws."

THALLIN.

During 1884 a chinoline derivative was made by Dr. Skraup in this same search after quinine substitutes,—which from yielding a very green color on reacting with ferric chloride and oxidizing agents was called thallin. The systematic chemical name of this base is tetrahydroparachinanisol, and the sulphate of this base is the salt commonly used as an antipyretic. Several of the salts of the base were investigated at the clinic of Prof. Nothnagel, and it is said to be very active in comparatively small doses. It is patented, and largely advertised, but in competition with other agents which have had these advantages, it has not come very largely into use. It appears to be a very active agent for reducing abnormal temperatures.

ANTIFEBRIN.

In 1853 Gerhardt discovered by a reaction between aniline and acetic acid a neutral body which was found to be phenylacetamide, or acetanilide. This substance was recently found to be an active antipyretic, and under the name antifebrin was, in 1886, very favorably reported by Prof. Kussmaul of Strassburg, as yielding very satisfactory results in comparison with antipyrin, whilst the cost is very much less, and the effective dose very much smaller. It is not patented, although the name, and perhaps a special quality under the name, is claimed as being proprietary. But it is also commonly sold now as acetanilide, of quite as good quality, and for but little over one-half the price it brings as antifebrin. That is, the two are identical except in price, and both are cheap.

SALOL.

This combination of about 60 p.c. of salicylic acid and 40 p.c. of phenol or carbolic acid, was first produced by Prof. von Nencki, of Berne, and investigated by Dr. Sahli, also of Berne,—the report of the latter upon the compound having been made in April, 1886. It was soon patented in Germany and the United States, and is now controlled by these patents. It is said to combine the properties and effects of its two constituents, and if so it is difficult to see why they should not be extemporaneously prescribed with the advantage of varying the proportions of the elements to meet the special requirements of varying cases.

ANTITHERMIN.

This is one of the two most recent additions to the long list of antipyretics. The systematic name given for it is phenylhydrazinlevulinic acid, and with such a constitution it is evidently nearly related to antipyrin.

Acetyl-amidophenol is the other of the two very recent antipyretics, and as yet this one does not appear to have received a common short name; and up to this time little appears to have been said in regard to these new agents.

No notice of prominent antipyretics should omit the mention of two of the oldest and best, although these may now be temporarily put aside for newer claimants to professional popularity. These two are veratrum viride and aconite.

In conclusion, it may be of interest to add a list of the prices at which these newer antipyretics are now sold by the wholesale druggists and to present specimens of each of them for inspection.

Sulphate of Quinine of the best makers at about	40c	per	ounce.
Tartrate of Chinoline	70c	"	"
Resorcin	30c	"	"
Salicylic acid, patented	20c	"	"
Kairin, patented	$2.00	"	"
Antipyrin, patented	1.25	"	"
Sulphate of Thallin, patented	1.75	"	"
Antifebrin, 30c per ounce, or as Acetanilide	15c	"	"
Salol, patented	40c	"	"

MATERIA MEDICA IN 1887.

By Edward R. Squibb, M. D.*

Section 3 of Article IX. of the By-Laws of the Association makes it the duty of the President to occupy the February meeting with some account of the progress made during the year in that department of the medical art or science in which he may have been specially interested.

In assuming this duty the writer is at a loss to know how much or how little of the pharmacology of the year is really progress in the right direction. So strong is the desire for novelty in all departments of human knowledge, that progression, in the sense of going forward, is not always improvement.

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* Read before the Kings County Medical Association, February 7, 1888.

That is, the apparent or seeming progress of one year is so generally checked and modified by the experience of those which follow, that any useful account of the advancement made should be, in large part, a consideration of what has been confirmed or refuted by continued observation and research upon the propositions and statements of preceding years. The writer will, therefore, not attempt to collect and enumerate the additions to the materia medica proposed during the past year, but rather try to glean from the too often conflicting experience of the year those statements which appear to be most trustworthy in regard to a few of the novelties which have lived through the past four or five years, and which give most promise of becoming established by general utility. Nothing original is to be offered, but only an attempt to sift out from the mass of public testimony that part which may be provisionally accepted as evidence for or against the substances which appear to be of present importance to the art of medicine. And even such conclusions are presented with hesitation and doubt, because it is by no means certain that all the important publications in regard to the agents under notice have been seen; and, again, because those which have been seen may not all be free from the bias of commercial enterprise. It has been very common within the past ten or fifteen years to control by patents all such new articles of the materia medica as could be patented, for the purpose of making money by them, and then the statements in regard to such patented articles are often the results of misdirected enthusiasm upon incomplete observation, procured in the money interest of the patents.

An illustration of this is so directly in the line of progress in the materia medica as to be worthy of a brief recital.

Piria discovered natural salicylic acid in 1838—salicine having been discovered by Leroux in 1830—and the acid was afterward made and investigated through all the years to about 1860, but always from natural sources. About 1860, Kolbe and Lautemann made the acid synthetically, and published their process.

This process was confirmed and repeated by many workers, among whom was this writer, so that the acid became more common, but still costly. About 1875 Kolbe, or some commercial house which represents him, patented his process for the acid, when all the makers in this country and abroad had to stop making it, or stand a lawsuit. Then began the florid statements in regard to its effects and uses, which all must remember.

An account of this process, and a summary of the early investigations with the acid, by this writer, were given in the *Chemical News* of London, vol. xxxiii., for 1875, at p. 46. It does not detract in the least from the great importance of the artificial production of this acid to say that not half the promises made concerning it have been realized, and that it would have sooner reached its true value, both in medicine and the arts, had it not been patented or not been lauded extravagantly, as a natural consequence of having been patented.

Commercially, the patent has been a great success, although it may be doubtful if Kolbe shared as largely in that success as he deserved. And the public benefit from the process has been much enhanced by the weakness of the patent. There were two or more large makers of the acid by the process when the attempt to enforce the patent was made, and these contested the patent, and kept the price within moderate limits during the long contest, until finally the patentees and their contestants made a compromise, and bound each other to a scale of prices so favorable to all that they have maintained them without break.

This patent expires about 1889, when a wholesome competition among the makers will undoubtedly soon reduce the cost to the public to perhaps one-third of the present price.

An item of progress in the true interest of the legitimate materia medica is realized when an English judge, in very decided language, refused to allow his court to be used as a medium for advertising quack medicines.

The case is given in the *Chemist and Druggist* of London, No. 396, for November 19, 1887, p. 639.

The proprietors of an American patent medicine sue a London patent medicine company in the High Court of Justice, before Mr. Justice Kay, to restrain the latter company from using a part of the name of the former. The agent of the first company declared on oath that his company had sold no less than 12,000,000 bottles of their medicine, and paid no less than £400,000 in advertising, and in one year alone had spent £100,000. He discovered that this enormous interest was being damaged by the company sued having got up their medicine in the same style, and having offered it in the streets by boys dressed up in variegated costume to represent the coat of many colors of Joseph, the medicine being Saint Joseph's

Oil, and the infringement or conflict being upon the use of the word "Saint," which was a part of the title of the plaintiff's oil.

The street boys sold the oil at a penny a bottle, and generally to the poor, upon the cry that "Saint Joseph's Oil conquers pain." This was the precise cry that the other Saint's Oil used, and now sought to have Saint Joseph restrained from using.

The Judge, without calling on counsel for the defence, dismissed the motion. He said he did not intend to be a medium for advertising quack medicines. He used the words "quack medicines" advisedly, and applied it to both parties in vigorous language, without stint or qualification; and all his remarks upon the case were wholesome and timely, placing the parties in their true light, and one they would not be likely to use in their advertising. And he wound up by saying that if any one chose to advertise this judgment he hoped they would add the words of caution which he now employed, namely, that no one should use either of the preparations except under medical advice.

One of the reasons for bringing this case in here is that it has not had a very wide circulation, nor much notice, possibly because the press lives so largely upon this class of advertisements. Anything of this kind is apt to lead tacitly to what the Duke of Argyll calls "the conspiracy of silence."

One journal, however, is outspoken, and after reading Mr. Justice Kay a pretty serious lesson, frankly shows its meaning in the following quotation: "To recur, however, to the sentence we quoted in the beginning of this note—namely, that 'this American company which, according to its own statement, is flooding the English newspapers with advertisements of this quack medicine'—we may take this opportunity of reminding judges, journalists, and others whom it may concern, that to the patent medicine advertisements of the past half century they and all England owe, in a very large degree, and more, probably, than to any other influence, the wonderful development of the cheapness and consequent power of the press, which is one of the greatest features of the Victorian era."

This seems equivalent to saying that it is good to foster quack medicines, although it may be at the expense of a legitimate materia medica, and of sound morality and truth, and health, because quack medicines impose an enormous popular tax, by which a powerful press is supported.

The chemical progress of 1887, which relates directly or indirectly to the materia medica, has been great, and chiefly in the direction of the production of artificial alkaloids.

CONINE.

A. Ladenburg has made one of the most complete and perfect syntheses yet recorded, in his artificial production of conine.

His work appears to have been in no sense or degree the result of accident or chance, but a patient, laborious building up from the elements. His paper is published in the Berlin *Der Deutsch-Chem. Ges.*, xix, 2579–2583, and an abstract in English is given in the *Journal Chem. Society* (London) for 1887, p. 160, and the Yearbook of Pharmacy for 1887, p. 76.

He first makes acetic acid from its elements, then by building upon these he gets α-picoline. Next, by the reaction between paradehyde and α-picoline, he gets α-allylpyridine. This latter, reacting with sodium, is reduced to α-propylpiperidine, which resembles conine very closely, but is not identical with it. Separated into two bodies by crystallizing the one from the other, he gets an active base identical in all respects with the natural base from *Conium maculatum*, or spotted hemlock. The artificial alkaloid converted into hydrochlorate is physiologically, as well as chemically, identical with the hydrochlorate of the natural alkaloid.

CODEINE OR METHYLMORPHINE.

In a paper entitled "The Chemistry and Pharmacology of Some of the Derivatives of Morphine," by Mr. D. B. Dott and Dr. R. Stockman, of Edinburgh, read at the British Pharmaceutical Conference at Manchester, and at the Ninth International Medical Congress at Washington, and published in the Year-book of Pharmacy for 1887, p. 538, the authors confirm the results of Grimaux in 1881, who first made artificial codeine from morphine, and showed that natural codeine was really methylmorphine. In this paper it is conclusively shown that the natural codeine from opium and the artificial codeine, are not only chemically but also physiologically identical so far as the action upon frogs, rabbits, and dogs goes, and it now only remains to be seen whether the inference that the therapeutical action is identical, be correct.

This paper also gives an account of investigations upon other derivatives of morphine, which are of interest and importance.

The artificial codeine—or perhaps rather the process for it—has been patented by Mr. Dott. But the same alkaloid is made in Germany by another process, which, even if also patented, will have the result of making a wholesome competition if codeine should come into any considerable use. As yet, it does not appear to have been much advertised.

SACCHARIN.

It is stated by several authorities that the new coal-tar derivative of Dr. Fahlberg, named saccharin, not saccharine, is quite innocuous in the human stomach, and does not increase the quantity of urine or of sugar in glycosuria, thus far showing by experience that it may be used without harm for sweetening the ingesta of diabetic patients.

But it has also been shown to be an antiferment of about the same power as boric acid, and MM. Aducco and Mosso show that it retards the action of pepsin and ptyalin when present in the very small proportion of 0.16 per cent. From this its effects on digestion in such proportion would be unfavorable, but perhaps not seriously so even in such a disease as glycosuria. Much smaller proportions than this are effective in sweetening food and drink, and retard digestion less.

FLUORINE.

Mr. A. E. Tutton gives in *Nature* for December 22, 1887, a full and most interesting account of the isolation of fluorine by M. Henri Moissan, whose paper on the subject appeared in the December number of the *Annales de Chimie et de Physique.*

This hitherto unsolved problem is one of the greatest achievements of modern chemistry, and some idea may be formed of the difficulties, from the fact that it required three years of almost incessant labor, through many failures; that most of the apparatus had to be of platinum, and that platinum tubes thirty-one inches long and half an inch in diameter were destroyed in each of the earlier experiments.

The element fluorine was obtained by the electrolysis of hydrofluoric acid. It is a gaseous element which attacks all known substances with such energy that there is nothing of which to make vessels that will hold it in a free state. Its union with hydrogen, even at a temperature of —23° C., is explosive.

ANTIPYRINE AND ACETANILIDE.

Of the numerous synthetical substances proposed and extolled as antipyretics, only two remain as being of much practical importance.

These are antipyrine and antifebrine, and they have been so recently discussed in their relations to fever that but little remains to be said under that head, but more upon their effects as analgesics or anodynes.

Antipyrine or oxydimethylchinizine was made by Dr. L. Knorr, of Erlangen, in 1884, and investigated by Filehne. It is readily soluble in water and alcohol, yielding solutions of but slight taste, and not disagreeable. The dose is from fifteen to thirty grains two or three times a day.

Antifebrine or acetanilide or phenylacetamide was made by Gerhardt in 1853. It was investigated as an antipyretic by Kussmaul, of Strassburg, in 1886, whose favorable report was soon corroborated by other observers. It is but slightly soluble in cold water, but freely soluble in diluted alcohol, brandy or wine. It produces a slight burning sensation upon the tongue, but in solution is not disagreeable.

The ordinary dose is from four to fifteen grains two or three times a day. Antipyrine is controlled by patents, and costs about $1.25 per ounce. Antifebrine, as a proprietary name, is controlled by patents, and when bought under this name it costs about thirty cents per ounce. The name acetanilide, for exactly the same substance, is not and cannot be controlled in any way, and under this name it can be bought for about fifteen cents per ounce. As acetanilide is about one-eighth the price of antipyrine, and effective in half the dose, it is far the more economical in use.

The two agents are about equal in power to reduce the temperature in fever, but acetanilide is generally believed to be less liable to produce profuse sweating and tendency to collapse, and to chill as the action passes off. Whether they are best used in small doses, frequently repeated, or in large, infrequent doses, seems as yet undecided.

Their effects in reducing fever temperatures by 1 to 5° F. is undoubted, and it is also beyond doubt that this reduction does, in many cases, but not in all, render patients with very high temperatures more comfortable during their administration. But that they have any curative effects, or any power over the duration, course, or termination of continued fevers is doubted by most writers. It is nevertheless difficult to resist the very rational conclusions of some careful observers, that when the agents are carefully and skilfully used only in cases of hyperpyrexia, and then only in such quantity as to reduce the temperature by one, two, or three degrees, in proportion to the elevation, or to within the moderate range of 101 to 103° F., they must have a favorable influence upon the gravity and termination of severe cases, if not upon the duration and course. If very high temperatures do not destroy life, nor very moderate temperatures indicate safety to life, still the latter are so much more desirable, from every point of view, that agents which command them must all be of value, antipyrine in some cases, acetanilide in others, cold sponging or wet pack in still others; and the most successful physician is he who, by discrimination or by trial, gets that agent which best fits the special case in hand.

All through the past year evidence has pretty rapidly accumulated to the effect that both antipyrine and acetanilide are useful analgesics in almost every variety of nerve pain. The pains of rheumatism, gout, neuralgias of various kinds and degrees, sciatica, lumbago, migraine and the pains of locomotor ataxia, all seem to have been effectively controlled by both agents, and apparently as well by the one as the other. But there is great discrepancy in the quantities used, some observers getting their effects from small doses, others from large ones.

COCAINE.

During the past year the applications of cocaine have practically ceased to multiply, and many of those of previous years are no longer heard of. The more conservative uses of it are, however, extending, and the increasing quantities sold suggest a question as to what becomes of it. Large quantities are undoubtedly made into proprietary "wines of coca" and other nostrums, but these take the cheaper kinds, and perhaps thus mitigate the growing vice of coca tippling. The current literature has been almost without evidence as to whether the cocaine habit is on the increase or not.

One fortunate circumstance seems to be that it is not attractive to as large a proportion of persons as opium or tobacco, and that its effects place it intermediate between these two narcotics.

As the effect of being a new agent wears off, and as it disappears from the public prints, it may be hoped that, as the material for a dangerous vice, it may be neglected and measurably forgotten.

In the uses of cocaine during the year the general fact has been abundantly supported that, wherever a mucous membrane or an absorbing tissue can be reached by it, the anæsthetic result is sure.

Therefore its utility in dysentery, gonorrhœa, affections of the nose and pharynx, and some affections of the stomach, are easily understood. But the use which throughout the year seems to have been most strongly emphasized is in the obstetric art, and this use is well summed up in an admirable paper of Mr. John Phillips, in the London *Lancet* for November 26, 1887, p. 1061, entitled, "The Value of Cocaine in Obstetrics." The author of this short and pithy paper concludes, from other competent authorities and his own experience, that in the vomiting in pregnancy, whether administered by the stomach, hypodermically, or by topical application to os, cervix and canal, it is a valuable agent, and in many cases will succeed when other agents have failed. That during the earlier stages of labor, especially in primiparæ, it materially assuages the pains, but neither quickens nor retards them, and therefore has no effect on the dilatation. That during the expulsive stages it is useless. That its utility in operations is probable but not proven, and that in sore nipples it relieves the pain of nursing without detriment to the nursling.

CONVALLARIA.

It seems to be about time to try to sum up the professional verdict upon convallaria. Proposed by Russian authorities in 1880 as having some advantages over digitalis, it did not attract much attention until 1883, when it became quite fashionable, and was much used as a cardiac stimulant or tonic. In general effect upon the heart it resembled digitalis, but was not cumulative in action, was more certainly diuretic, and less liable to disorder the stomach. While resembling digitalis in its effects, these effects were the result of a cause different from the cardio-inhibitory excitation of digitalis. It was therefore adapted to a different class of cases from digitalis, and these not easy to recognize until convallaria was applied with success where digitalis had failed. It was also shown that it was not as dangerous from overdosing as digitalis. That digitalis is liable to cumulative activity, is the general statement of the books, but if it has any such tendency it is so easily seen that it is doubtful whether the immunity of convallaria from any such risk gives it the claimed advantage. Most of these points, made in the journal literature of 1883-4-5, seem to have been supported by practical experience, and yet convallaria has largely gone out of popular use, while digitalis has maintained its ground. Many good observers continue to use both, but in most cases use digitalis first, and only change in case it fails to meet their indications. Hence, convallaria may be considered to have settled into the role of an useful alternate for digitalis, thus adding to the resources of the general practitioner.

IODOFORM.

Since the enthusiastic general introduction of iodoform into medicine and surgery by Van Mosetig-Moorhof in 1879, the substance has been very generally and very successfully used as an unirritating anodyne application, under which unhealthy and unnatural processes are corrected or retarded, and healthy action substituted.

Much of its beneficial activity has been attributed to antiseptic action or power, and it has been generally supposed that under its use septic processes were impossible. While its general and special utility has been so widely accepted as to be well-nigh universal through six years of increasing application and reputation, and while there is no reasonable doubt that its great reputation is entirely sound, its chief mode of action has been this year called in question and denied by good authority. Its two prominent characteristics were that it was antiseptic and anodyne, these being its principles of action. About a year ago C. Heyn and T. Rosving, of Copenhagen, published a paper which has attracted much attention by claiming, on the basis of careful research, that iodoform is not antiseptic, but that micro-organisms will grow freely in it. These results were very promptly and very rudely called in question, and denied, but thus far they do not appear to have been controverted by counter-research.

The results of the Copenhagen investigators were foreshadowed by others before them, but not on such grounds.

In whatever way this dispute may be ultimately settled, it can hardly disturb the established utility of the substance. But it will be a shock to find that it has not been killing germs all this time, but has been curing in some more peaceful way.

IODOL.

In 1885–6 Drs. Silber and Ciamician, of Rome, made a combination of iodine with pyrrhol, a tetraiodopyrrhol, which they called iodol.

It contained 85 to 90 per cent. of iodine, while iodoform contained 96 per cent., and was similar to iodoform in many respects, but devoid of odor. Dr. Mazzoni, of Rome, investigated the new substance, and pronounced it a powerful antiseptic, with anæsthetic action.

It seemed applicable to all the uses of iodoform, but had the great advantages over iodoform of being free from odor, and not poisonous under any ordinary quantities. It has been considerably used as a substitute for iodoform, especially in Berlin and Vienna, and the reports upon its use are very generally favorable. It is, however, too early to know whether its advantages over iodoform will be sustained by general experience. And if iodoform should be proved not to be an antiseptic, it would follow as a probability that iodol is not.

PAPAIN.

Papain, the vegetable digestive ferment obtained from the unripe fruit of *Carica papaya*, or Papaw, has been again brought into notice as an active alternate to pepsin. While pepsin is inactive in neutral and alkaline conditions, papain is active, and therefore, in using the latter it is not necessary that any free acid should be present. Pepsin with acid, and papain without, are claimed to be equal in activity and power, and if so, there are quite a number of conditions to which papain is applicable to which pepsin is not.

It, therefore, appears rational that in dyspepsias, which are not relieved by pepsin, papain may, as is asserted, be useful, and thus become an additional resource for the practitioner. An admirable paper by E. J. Eastes on papain may be found in the *Pharm. Jour. and Transactions*, London, for July 11, 1885, p. 45, where a good summary up to that date is given.

PARALDEHYD.

Although paraldehyd has not sustained the promise of its early advocates, it is still used as an alternate hypnotic. The statement that it has no stage of excitement has been successfully called in question, but when given in full doses the excitement is so slight and so short that it is difficult to detect, and no practical disadvantage. The statement that it is safer than chloral, in having no depressing action on the heart, seems to be sustained by experience, but it is not always free from some degree of after disturbance. The great drawback to its use that it is disagreeable and even difficult to administer has not been overcome, and it has not been shown to be effective when chloral has failed, but has been shown to be available when chloral was counter-indicated. The dose of one to two fluidrachms requires about twelve times the quantity of water for easy solution, and this seems to be about the best way to administer it.

It is singular that the original observation of Cervello or Cercello, of Palermo, in regard to its antagonism to strychnine has not been noticed to have received useful recognition, nor to have been refuted. Dujardin-Beaumetz, like Cervello, gave the paraldehyd to rabbits first, and then the strychnine, while Bokai gave it to the rabbits mixed with the strychnine. Such an antagonism is not available in the treatment of strychnine poisoning. It seems hardly possible that such an important antagonism has not been farther investigated, and much more probable that the writer has missed finding the records.

In human cases of strychnine poisoning Bokai suggests 6 to 10 grammes of paraldehyd twice daily, until prolonged sleep is procured.

SALOL.

The substance salol is hardly old enough as yet to warrant any safe conclusions in regard to its value. The best account of it met with in English is in a paper by Mr. John Moss, F.I.C., F.C. S., published in the Year-book of Pharmacy for 1886, p. 526, his information having been chiefly derived from *La Semaine Medicale* of April 14, 1886.

Made by Von Nencki and investigated by M. Sahli, both of Berne, it was presented to the local district Medico-Pharmaceutical Society, on April 6th, 1886. The process of making it has not been published by the maker, but a process has been published by C. Kolbe. It is controlled by patents both here and in Europe. It is a combination of salicylic acid and phenol.

It appears to consist of 56 to 62 per cent. of salicylic acid and 44 to 38 per cent. of phenol, and chemically it is said to be a salicylate of phenol (Sahli) or salicylate of phenyl (Moss).

It is a white, coarse, crystalline powder, with the odor and taste of wintergreen in which carbolic acid is suggested. It is insoluble in water and acid liquids, but soluble in diluted alcohol, and in alkaline liquids. It is therefore said to pass through the stomach undissolved, but to be dissolved, dissociated and utilized in the intestines, and excreted as urate of salicyl and sulpho-phenol.

It is proposed as a substitute for salicylate of sodium and phenol in all conditions to which either is applicable, and it certainly has the great advantage over both in facility of administration.

The doses advised are about 30 grains three or four times a day, and each of such doses represents about 17 grains of salicylic acid and 13 of carbolic acid—very effective quantities of each.

It has been effectively advertised as a novelty, and, as usual, the list of affections in which it was used and extolled by Sahli and others is long and hardly rational. In solution it can hardly fail to be antiseptic and antipyretic if dissociated into its elements, and it is therefore very rationally applicable to the treatment of rheumatism, sciatica and neuralgias.

Most of those who have written upon it have used it as a substitute for sodium salicylate, and have compared it with that salt, but these comparisons are conflicting, and it is easy to see are not yet free from interest or prejudice.

It certainly has one advantage over the sodium salt, in not producing a primary disorder of the stomach. Being insoluble in watery fluids, especially when these are acid, in the stomach, it passes through that viscus inactive, and only becomes soluble in the small intestines. But when pushed it does disturb the digestion secondarily as the sodium salt does. Farther observation is necessary to show that it has any other advantage over the sodium salt, for which it is an alternative in about the same doses.

STROPHANTHUS.

In the *Pharmaceutical Journal and Transactions* (London) of January 4, 1873, p. 523, is an abstract of an article from the *Journal of Anatomy and Physiology* (Edinburgh), vol. vii., on "The Kombé Arrow Poison (Strophanthus) of Africa. By Thomas R. Fraser." This very interesting account of strophanthus is the first notice of it that has been found, and seems to be the beginning of Prof. Fraser's published investigations of the substance since brought into such prominent notice. He then obtained a crystalline active principle from the seeds, which he found to be a glucoside and called it strophanthin.

The next publication met with is a paper by E. Hardy and N. Gallois in *Comptes Rendus*, vol. lxxxiv., p. 261, in 1877, where the active principle is described as being neither an alkaloid nor glucoside. The hairs removed from the seeds were found to contain an alkaloid, but devoid of the peculiar action of the seed on frog's heart.

Then, with one or two unimportant notices, nothing has been noticed on the substance until the meeting of the British Medical Association at Cardiff, July 28, 1885. At this meeting Prof. Fraser read a paper on "The Action and Uses of Digitalis and its Substitutes, with Special Reference to Strophanthus (Hispidus?)."

This very interesting paper is published in the *British Medical Journal,* vol. ii., for 1885, p. 904.

In this paper Prof. Fraser states that his investigations of strophanthus began in 1870, and that he had been preceded by M. Pelikan, of St. Petersburg, in 1865, and by Drs. Hilton Fagge and Stevenson in the same year. The author says that want of the material, and other unavoidable circumstances, interrupted his investigations for some years, but that in view of the probable importance of the subject he had resumed it when able to do so. He regards the action of strophanthus as exceedingly simple. It may be described as a simple muscle-poison to the striped muscular system, and because the heart receives a larger share of any circulating muscle-poison it is more affected by it. In lethal doses it stops the heart in extreme systole, and the rigidity of the contraction passes into the rigor of death. The changes produced by moderate doses upon the heart's action are those produced by digitalis. It causes a rise in the blood-pressure, but in a less degree than digitalis, and like digitalis it is actively diuretic.

Therapeutically, it was not very thoroughly compared with digitalis, nor was its active principle very thoroughly compared with digitalin, except upon the frog's heart, but upon the frog's heart it was some sixty times more potent than digitalin. The author concludes that the action of strophanthus on the heart is much more powerful than that of digitalis, while the action upon the blood-vessels is much weaker, and upon this observation he reasons that it may be better and safer than digitalis, because the latter by greater contraction of vessels antagonizes a part of the increased power of the heart by increasing the resistance to it in the vessels. By this action digitalis becomes an hæmostatic, an action that is wanting in strophanthus.

Both are valuable diuretics, and as strophanthus does not much increase the blood-pressure, it is argued that this blood-pressure is not the essential factor in diuresis.

From his limited application of the two agents he is led to believe that sickness and gastro-intestinal disturbance are not produced so frequently by strophanthus as by digitalis.

He occasionally used strophanthin hypodermically, but found it sometimes produced inconvenient irritation at the point of injection.

This is a very unsatisfactory *resumé* of this important paper, but it may serve the purpose of making a *resumé* of what has since been written on the subject intelligible. The subject attracted much attention, and a large amount of testimony has been published during the past two years and a half, and therefore it will be difficult to discriminate between the accurate and the loose observations so as to sum them up fairly.

In the *British Medical Journal* of September 17, 1887, Vol. II., of 1887, p. 620, under the head of "Notes on Strophanthus, by K. N. Bahadhurji, M. B., B. S., Lon., (From the Pharmacological Institute, Berlin)", there is an important paper wherein the author shows that strophanthus is something more than a simple muscle-poison, and that the nervous system is markedly affected by it, and this not secondarily through the heart and circulation, but primarily, because in small doses, which do not appreciably affect the heart, nervous symptoms are observed. In one case there was paralysis of the animal, followed by tetanus, in which the animal remained for three days, the heart being not the least affected.

This conclusion, that strophanthus is not a mere muscle-poison is also reached by a Russian authority, Dr. Kazem-Bek, who gives evidence that the action upon the heart is, at least partly, through its nerves. (See London *Lancet,* December 3, 1887, p. 1136.)

So much has been written upon the therapeutic effects of strophanthus, from Prof. Fraser's investigations down to the present time, that no one can doubt its potency and value as a heart tonic, and its useful applicability to both functional and organic derangements of the heart. That it has been badly managed, and that it is simply impossible that it could have done all that is credited to it in organic diseases of the heart must be admitted, for no new remedy escapes this history; but whether, upon a fair average, it has any advantages over digitalis seems doubtful.

That it is not a duplicate of digitalis is very evident. Each agent has a power and applicability of its own, and neither is likely to supplant the other. Neither is it a duplicate of convallaria, although much of the testimony in regard to it is very similar to what was written of convallaria in the early part of its therapeutic application. Hence, as an addition of real value to the materia medica, it is at least of present importance, and accumulating experience alone can decide whether it has sufficient individuality to sustain its present importance. Many instances are reported in which it has been successfully applied after digitalis, convallaria and other agents had failed, and a few in which other agents were effective after it had failed.

Several writers of eminence, whose cases must have been both well understood and well observed, report favorably of its control over the threatened heart failure in exhausting diseases, such as typhoid fever, but do not compare it with digitalis in a similar class of cases. In many cases, where patients were dying of dyspnœa, "water-logged," from either primary or secondary cardiac insufficiency, it has been of great service. Its diuretic action is at least as good as that of digitalis, but either one will at times fail when the other will succeed, and not infrequently both fail. It is alleged to have a great advantage over digitalis in not being cumulative, as digitalis is said to be. This cumulative action of digitalis is perhaps generally understood to be some degree of toxic explosion, but as any definite account of such action from digitalis has been sought for in vain in all the comparative effects of this class of agents, it must be extremely rare, and perhaps it may be a legend handed down by the books from times when digitalis varied more in quality, strength and dosage than at present, or when the relation between cause and effect was less accurately observed. If by cumulative effects is meant the liability, after a time, to disturb the stomach and cause nausea, vomiting, etc., then the records seem to show that strophanthus does this as often as digitalis. One point recently gained in the use of strophanthus should be rigidly adhered to. A tincture of the seed only should be used, and this of the strength of 1 part by weight of the seeds to 19 parts by weight of the officinal diluted alcohol. That is 1 in 20 by weight. This is sufficiently near to Prof. Fraser's more recently adopted strength, as recommended by Mr. Wm. Martindale, of London. The dose of such a tincture is stated to be 5 to 10 minims three or four times a day, that is, 15 to 30, or 20 to 40, minims in the twenty-four hours, but it has often appeared that 2 to 3 minims every two or three hours, until the heart was steadied, was a better dosage, and then to vary this in either quantity or time to suit each case. The doses have been found to be best given in half a wineglassful of water, mixed at the time of taking, and when so given the effect is not unfrequently felt by the patient and at the wrist within fifteen minutes. The tincture is quite bitter, and for hypersensitive patients capsules may be half-filled with loose liquoric powder and the dose dropped upon this.

The active glucoside strophanthin has been used hypodermically, but with doubtful advantage, at least until it can be made better and at lower cost. At present the price is about ninety cents per grain; and it is in a semi-liquid state difficult to manage with accuracy; and is so potent as to be very dangerous. Only one or two manufacturers are as yet making it, although three years have passed since Prof. Fraser published his process and description.

Prof. Fraser has always published freely all that he knew of strophanthus and strophanthin, and seems to have taken pains to keep the subject freely open to the profession in every possible way, so that no one could claim any exclusive proprietorship in the drug or its preparations.

URETHANE.

Urethane or ethyl-carbamate was proposed as a simple hypnotic by O. Schmiedeberg, Professor of Pharmacology in the University of Strassburg, in a paper "On the Pharmacological Action and Therapeutic Application of Some Ethereal Salts of Carbamic Acid." This paper is found in *The Practitioner,* for 1885, vol. xxxv, pp. 275–328–417.

Its effects as an artificial hypnotic compound were foretold from its composition when it was made and applied, and justified the expectations of the author. His paper closes with the following paragraph:

"Urethane can therefore be used in general as a hypnotic, and we foresee that it will frequently be of special use in those cases where the smell and taste of paraldehyde interfere with its use, and where the action of chloral hydrate on the heart, vessels, and respiration must be avoided. This compound is no more a universal remedy to produce sleep than any other substance, but a consideration of its pharmacological relations will enable the practitioner to choose the cases correctly in which a satisfactory result is to be expected from it; while tentative trials without any definite plan will here, just as in the application of medicines in general, lead to the disappointment of cherished expectations."

Von Jaksch, of Vienna, reported favorably upon it in 1885—see abstract in the *British Medical Journal* for 1885, vol. ii, p. 611—having used it in 20 cases 110 times.

Riegel, of Vienna, used it 67 times in 27 cases, favorably, as a simple hypnotic, without anodyne effect.

Dr. A. S. Myrtle, Harrogate, used it in over 50 cases, with general satisfaction.

MM. Mairet and Combemale, of Paris, used it 300 times in 37 insane patients, with general success.

Mr. J. F. Paley, of Brighton, England, used it in 10 cases with benefit in about half the number, but Dr. Uthoff and Mr. Scott at the same time reported that in several cases it had given no satisfactory results. And Dr. Mackay had seen no marked benefit from it.

Dr. Robert Saundby, of Birmingham, reports 2 successful applications. Sir E. H. Sieveking, of St. Mary's Hospital, used it in 12 cases with general success.

Dr. Coze reports many experients on animals (the *British Medical Journal*, vol. ii, 1886, p. 176), wherein the antagonism of urethane to strychnine was conclusively shown, and Dr. Coze asks for clinical application in convulsive conditions.

Mr. William Thomas Jackman, F.R.C.S., etc. (London *Lancet*, vol. i, 1886, p. 1112), reports a case of traumatic tetanus treated first with chloral with some benefit, but afterward with urethane alone, with prompt relief and final recovery.

Dr. Emil Kræpelin (the *British Medical Journal*, vol. ii, 1886, p. 268, from *Neurologisches Centralblatt*, March 1, 1886), reports the use of urethane in about 200 instances, most of them cases of insanity, with very general success. He thinks it is a simple hypnotic of no great energy, which in cases of great excitement is of little value. In delirium tremens it failed entirely, and for the relief of pain is of no use whatever. In his general success with it doses of 1 gramme (15.5 grains) were effective in 54 per cent. Doses of 3 grammes (46.5 grains) were successful in 70 per cent.

Drs. Otto and Kœnig used it in a large number of insane patients, often in very large doses, and found it frequently very serviceable.

Dr. J. B. Andrews, of Buffalo, N. Y. (*American Journal of Insanity* for October, 1886), used it upon himself when in health, and then upon more than 20 cases, in doses of 7 to 60 grains. He found it generally successful, and most successful when in a single full dose.

Dr. E. Braun (London *Lancet*, vol. ii, 1886, p. 411, from the *Eira*), a sufferer from insomnia attendant upon "heart disease," tried urethane on three successive evenings in doses of 2 grammes—2 grammes at first and 1 gramme additional in an hour—and on the third evening 3 grammes in one dose, all without success.

Dr. Hans Rottenbiller (*Amer. Journ. of Med. Sciences*, vol. i, 1887, p. 224, from *Centralblatt für Nervenkrank*, etc., No. 10, 1886), used it subcutaneously in 14 patients by 240 administrations; with 7.5 to 15 grains he secured about four hours' sleep the first few days, then only one or two hours. From 30 to 60 grains, six to eight hours' tranquil sleep in 8 patients. In maniacal excitement it failed altogether, and paraldehyde was used with success. All his patients were insane, and his results were generally favorable.

With the exception of single cases and editorial comments, these are all the important reports that have been noticed in regard to urethane; and from these the following conclusions are drawn:

Urethane appears to be a simple hypnotic of too little sedative power to overcome any great degree of nervous excitement, but of sufficient power to be very useful in a large class of cases of simple primary insomnia.

It is in no very useful degree anodyne or analgesic. That is, when insomnia is secondary, or the result of pain or other serious peripheral disturbance or irritation, it is almost useless. In action on the sensorium it is like paraldehyde, but less powerful, while both are much inferior to chloral in power.

Of all the hypnotics it has much the least disturbing effect upon the functions of the organism, and therefore the sleep obtained by it is most natural, and the most refreshing and restful, and its effects are least counteracted by subsequent hurtful reaction, yet it is not free from disagreeable reaction when used in large quantities.

In breaking up a simple habit of insomnia, the original cause of which may have passed or become weakened, and in concentrating fitful, short and broken sleep into that which is more sound and continuous, it is often very effective, and this without the subsequent headache, loss of appetite, disturbed digestion, etc., of the more powerful agents of its class. It is transient in effect, and soon establishes a tolerance which requires larger and larger doses until it becomes as disturbing in its after effects as other more powerful agents, but, unlike these, it does not appear to be toxic in any quantities up to 12 grammes, 186-grain doses.

The effective dosage seems to vary from 15 to 60 grains; and although many reporters obtained excellent results from 6, 7 and 8-grain doses, these had so often to be repeated in other cases before any effect was reached, that there does not seem to be any economy in exceptionally small doses, especially in view of the observation of Dr. Andrews, of Buffalo, that its best effects were best secured by single full doses half an hour before the desired effect, this half-hour to be passed under the conditions of quiet and repose which most favor sleep.

The administration of urethane is most simple and easy. It is freely soluble in twice its weight of water at ordinary temperatures, although some good authorities describe it as insoluble, and the solution, even when concentrated, is not very disagreeable.

When the dose is diluted with half-a-wineglassful of water or more, it is easily taken even by the fastidious, and does not offend the stomach. Given upon an empty stomach, it is often very rapidly absorbed, and then yields its effects within fifteen or twenty minutes. When the stomach is slow, or in a passive condition, the effects are proportionately less prompt.

Some have reported using it hypodermically with success, as it does not seem to be irritant when placed under the skin; but the dose being large, the solution has to be dense in order to get it within convenient limits for hypodermic use. The observer who used it most largely in this way, did so for economy sake, because the substance was so costly—say over two dollars per ounce; but within the past year or two, when there were several makers of it, the price has been moderate, not over fifty to sixty cents per ounce.

As might have been expected from the character of Prof. Schmiedeberg, he has never attempted to patent or control urethane in any way, nor has he allowed any one else to do so. He described the process for making it fully and freely, and very soon it was made by several makers.

Throughout this note urethane is written with a final *e*, in respect for Prof. Schmiedeberg's authority, as it must be admitted that the author of the name has the right to spell it as he pleases, and probably has reason for spelling it as he does. But the common usage, in English at least, has dropped the final *e*, and it is now written and pronounced urethan.

DRUMINE.

In 1886 Dr. John Reid, M. A., of Port Germein, South Australia, claimed to have discovered an alkaloid in *Euphorbia Drummondii*, which was a local anæsthetic like cocaine, and which he called drumine.

On January 6, 1887, Dr. Alexander Ogston, C. H., of Aberdeen (see the *British Medical Journal*, vol. i, 1887, p. 451), received from Dr. Reid forty grains of the new alkaloid for trial. He carefully tried it upon his own person, upon an assistant, and upon two patients, without any perceptible effect. He therefore concludes either that the substance must have decomposed in transit, or that Dr. Reid is mistaken in his statements concerning it.

GLEDITSCHINE.

During 1886 a Mr. Goodman, veterinary surgeon, claimed anæsthetic effects from a poultice of the leaves of *Gleditschia triacanthos*, the common honey locust; and Dr. Allen M. Seward of Bergen Point, N. J., claimed to have obtained an alkaloid with anæsthetic action from leaves of the tree received from Mr. Goodman.

Dr. J. H. Clairborne, Jr., of New York, received from Dr. Seward a solution of this new alkaloid, and finding it to be a very active local anæsthetic, wrote two papers on the subject (the *Medical Record*, July 30, 1887, p. 127, and for October 1, 1887, p. 445), from whence the above statements are made.

These attracted prompt attention, and in the same journal for August 13, p. 180, Dr. Herman Knapp, of New York, has also an important paper extolling the new anæsthetic. Other papers and notices soon followed, and the demand for the two per cent. solution was very active, at very high prices, until November, when Dr. F. G. Novy, of Ann Arbor, published a paper in the *Pharmaceutische Rundschau* of Dr. Fr. Hoffmann for that month, p. 248, in which Dr. Novy showed that the two per cent. solution of gleditschine or stenocarpine was a solution of about six per cent. of hydrochlorate of cocaine, with five-tenths of one per cent. of sulphate of atropine, the solution having been protected by salicylic acid.

HOPEINE.

Early in 1886 Dr. W. Williamson, of London, claimed the discovery of an hitherto unknown alkaloid in American wild hops, which he called hopeine, and described its action as being similar to, but not identical with, morphine. This novelty was produced and controlled by the Concentrated Produce Company (Limited), of London, who represented that it was not present in the ordinary hops of the markets, but only from American wild hops. When on trial in France the new alkaloid was suspected, and not long after was shown to vary in different samples from the original source. Then several chemists found it to be at times almost all morphine, and at other times mixtures of morphine and cocaine.

Like gleditschine, it attracted a great deal of attention, and the literature of the subject is pretty extensive, and winds up with the authoritative statement of Prof. Asa Gray, that although he had seen the hop plant growing wild in America, yet never in such a way that he could have gathered a pound of the dried hops.

COST OF MAKING FLUID EXTRACTS.

In continuation of the subject of Fluid Extracts by Repercolation from p. 993, it may be useful briefly to discuss the cost of making such preparations by the large manufacturer and the dispensing pharmacist, especially as this element of cost has been recently treated of in some pharmaceutical societies and journals.

Mr. G. H. C. Klie, in a paper read before the Drug Clerks' Association of St. Louis, advocates the making of this class of preparations by the pharmacist as a source of pecuniary profit, and gives a table showing a very large saving in the cost to the pharmacist. *The Pharmaceutical Era* for December, 1887, p. 437, rather doubts the pecuniary profits shown by Mr. Klie, but shows an economy and profit which is far more important in that by such a practice the pharmacist keeps himself and his assistants practically acquainted with the art of pharmacy, and interests them in the progress of their art. And besides, the practice renders them independent of the large manufacturers who are constantly tending to monopolize the art of pharmacy.

To this excellent argument in favor of the practice may be added the still stronger one that it gives the pharmacist entire control over, and responsibility for that which he dispenses, and thus affords an opportunity by personal knowledge and skill to win that reputation which is the best and surest, if not the only proper basis of success in his very important calling. If he makes his preparations himself he knows exactly what quality of drugs and what quality of skill go into them, and the responsibility thus assumed ultimately becomes his profit, both in reputation and in money. The importance of the pharmacist in any community is almost if not quite equal to that of the physician, because his calling takes him directly to the bedside of the sick, and on the quality of his products both physician and patient often have to rely. His character is a most important element in every medicine he supplies, and he loses the opportunity to make character every time he dispenses supplies not made nor verified by himself. He is one of the few men who cannot live long in any community without making character of some kind, and no opportunity for making good character can be wisely allowed to escape. Knowledge of his business, and skill in applying this, come first, and next his fidelity and truth to his trust. These are judged of more by what he does than by what he says, or by the sign over his door, and very soon a part of his personal character and ability go to the bedside as a part of every prescription he dispenses and with every simple he supplies, there to be put to the crucial test. Then just in proportion to the character he has earned and to the way this character stands the constantly repeated application of this test, will he be able to charge,—and be justified in charging, for his work. That pharmacist who has gone in and out before his community long enough and right enough to establish a moderate degree of trust in the ability and fidelity of what he does, can easily command the full value of his work, and can get full value, however much his character and work may have cost him. Therefore it is that he should get,—and can justly get, double the price for any fluid extract or tincture made by himself, over any which he can buy, and in this way make both reputation and money.

Apart from these considerations, however, fluid extracts are no exception to the general rule that the larger the scale upon which any manufacturing process is conducted the less expensive is the product, and if this be so Mr. Klie is mistaken in his figures and his line of argument, though he is from other premises entirely right in his conclusions that well educated pharmacists should make their own fluid extracts, tinctures, etc., rather than buy them.

The actual cost of making fluid extracts depends mainly upon the quality of the materials used, and the knowledge and skill in using them. Next upon the scale of operations, and finally upon avoiding loss or waste in the menstrua used for exhausting the drugs.

This cost will of course vary with the cost of the drug, the menstruum and the apparatus and labor. A drug of high or low cost may have a menstruum of high or low cost, may have a high or low cost for labor, and may have a great or small loss of menstruum, and therefore the cost of the product bears no constant relation to the cost of the drug, or even to the combined cost of the drug and menstruum.

The ordinary list of fluid extracts in common use fall into natural groups of somewhat similar cost, though the elements of cost may vary very much, and it may be sufficient for illustration to take an example from a group of high cost, and another from a group of low cost.

Cubeb, ipecacuanha and lupulin are of high cost, because the drugs, menstrua and labor are all of high cost, and they are therefore exceptional in cost of production. But ergot may be taken as a better example of the class of costly fluid extracts. The best ergot comes from the rye districts of Spain, and is best yielded by the damp valleys and in wet seasons. Hence the crop is precarious in both quantity and quality,—varying much in price and therefore subject to "cornering" speculations. Bought in Spain it varies in different years and under different speculative tendencies, between 22 and 62 cents, but the average is perhaps not over 35c per pound. Great care is needed in buying to avoid getting an admixture of old ergot that had been held for price and brought over from other years, and no little skill and experience is required to detect such practices. The ergot is then held open till cold weather, to avoid heating and the attacks of insects, and then is shipped by quickest transportation. On arrival it is at once opened and spread out to dry, otherwise it would heat and mould and be attacked by insects. By this drying it loses about 10 p.c. in weight. It is then put in tight vessels with sheets of paper wetted with chloroform at top and bottom, and through the ergot, using about a pound of chloroform to each 500 lbs. of ergot. This effectually prevents the attacks of worms, while the ergot is being gradually made into its preparations. Before being ground it is passed through a shute crossed in different directions by large magnets, and these take out the nails and tacks and other small pieces of iron and steel accidentally or fraudulently in it sometimes to the amount of a quarter of one per cent. Next it is screened in a blast of air, and this process takes out 1 or 2 p.c. more of dust, chaff, chips, etc. Then it is ground only as the percolators are ready to receive it, because it is known to deteriorate rapidly when ground. In all this management, including the grinding, the loss is not less than 13 to 14 p.c., and the labor, chloroform, grinding, etc., are not less than 4c. per pound. Therefore, ergot costing 35c. in Spain, and say 1c. per pound additional for freight, insurance, and other transportation charges, will actually cost when ready for percolation not less than 45c. per pound.

Then 1⅛ pounds of this ground ergot is required for a pint of fluid extract, the pint weighing nearly a pound and an ounce, but when put up in bottles yielding a little short of a pound. This makes the ergot in each pound of fluid extract, of the strength of minim for grain, cost about 51c. The menstruum used consists of 86 parts diluted alcohol and 1 part of acetic acid, and costs for the constituents about 16c. per pound, or for that proportion of a pound which is present in a pound of the fluid extract, thus bringing the cost of the materials present in a pound of fluid extract, to about (51 + 16 =) 67 cents.

But this is by no means all the menstruum that is used in making a pound of the fluid extract. For practical exhaustion of the drugs in making fluid extracts, about 6 times the weight of the drug in menstruum is required, and less than one-sixth of this is present in the finished fluid extract. If the process of repercolation be used the other five-sixths are used over again with a loss which compared with any other process is small, but which at best is not less than one-eighth of the total menstruum used, or three-fourths of the weight of the finished fluid extract, and this upon a scale of 200 pounds at an operation, when the alcohol is recovered from the exhausted residue as closely as possible by distillation. If upon a smaller scale by repercolation the loss is slightly greater. But if by the Pharmacopœia process, wherein the weak percolates are evaporated off, the loss of menstruum is over four times greater,—that is, about five-sixths of the total menstruum is lost instead of one-eighth. In the case of ergot this loss of one-eighth adds 12c. to the cost of menstruum in a pound of fluid extract and brings the cost up to (67+12=) 79c. for the materials represented. Another large element in the cost of making fluid extracts is the quality of the labor used, there being little use in having good materials if poor, cheap labor be employed. If intelligent skilled labor be used it will cost not less than $2.25 per working day for each person, and not less than 25c. per day additional for the superintendence of a foreman. Then beside the labor of making, there is labor of bottling and putting up, and in this process, if full weight be put in each bottle, 104 pounds of fluid extract will be required to put up 100 one-pound bottles. And if in bottles of less than a pound the loss is proportionately greater. It is impossible to compute the cost of this element of labor with accuracy, but it may be fairly estimated at 12c. per pound, and then 79+12 is 91c. per pound.

Then there is the cost of a bottle,—cork,—wrapper and three labels, and for packing which together is not less than 7 cents, making 98 cents.

The rent, interest on capital, insurance, taxes, office and other general expenses of manufacturing establishments where steam power is used, are estimated at 15 p. c. on the cost of materials and labor used, and this brings the cost up to (98+15=) $1.13 per pound.

These elements of cost for a pound of fluid extract of ergot may be divided into groups as follows :

1⅛ pounds of ergot costs in Spain	39
Cost of importation	01
Loss by drying, cleaning and chlorform management	10
Grinding	01
Menstruum	28
Labor and superintendence in making and putting up	12
Bottle put up, and cost of packing for transportation	07
	98
General expenses of manufacturing establishment as interest on capital, rent, insurance, taxes, etc., 15 p.c.	.15
Total net cost	$1.13

In consideration of the knowledge, experience and responsibility involved in making this class of preparations, if well made, the maker is justly entitled to a profit of 25 to 30 p.c. and the business then is not overpaid.

The price of fluid extract of ergot is $1.65 per pound, and from this a discount of 10 p.c. is made on 95 p.c. of all that is sold by this maker. This reduces the available price to $1.49 or 32 p.c. over the net cost of making.

In such materials as can be obtained of the best quality with less difficulty and trouble the profit is less in proportion, and there are very few articles as troublesome as ergot.

Then at the opposite extreme of the list there is a class of fluid extracts the materials of which are of low cost, and can be had of the best quality with comparatively little trouble or expense. As examples of this class buckthorn and cascara may serve as illustrations.

The best quality of either of these barks can be had in the open markets in any quantities, if large, at 7c. per pound. Little or no garbling is needed,—there is no loss by drying,—no difficulty or cost in preservation, no haste to make up after grinding, and the loss in grinding small.

The menstruum here is 25 p.c. alcohol, 5 p.c. glycerin and 70 p.c. water, and it is therefore less costly than the officinal diluted alcohol, and the amount present and lost cannot be estimated at over 21c. for each pint of fluid extract.

The detail of cost, grouped as before, would then be as follows :

1⅛ pounds of buckthorn or cascara bark	.08
Grinding and loss	.02
Menstruum	.21
Labor and superintendence in making and putting up	.12
Bottle put up and cost of packing for transportation	.07
	50
General expense of manufacturing, as interest on capital, rent, insurance, taxes, etc., 15 p.c	.08
Total net cost	.58
Profit 30 p.c	.18
	.76

The price of these fluid extracts is 85c. per pound, less 10 p.c. discount when sold in quantity making a net available price of 76.5c. per pound.

It will be seen from these illustrations that the most variable element of cost is the cost of the drug, and that the maker can largely increase his profit by buying cheap drugs. Russian, German or Spanish ergot may easily be bought at two-thirds of the cost given above, especially if old ergot be accepted, or if bought ground, and the same is true of buckthorn and cascara; and the fluid extracts from the cheap drugs cannot be discriminated either by the sensible or chemical properties.

The most variable element of management is the loss in drying and grinding, and both these elements vary in the cost of each special drug.

The element of the menstruum varies principally from the varying proportion of alcohol it contains. If as in such articles as buchu, cannabis, cubeb, etc., the menstruum be strong alcohol the cost in each pound of fluid extract will be about 48c. If of 2 parts alcohol and 1 part water, the cost will be about 38c. If of officinal diluted alcohol about 28c., and if of 25 p.c. alchol, about 21c.

The other two elements of labor and bottle are fairly uniform, though less easily estimated than the preceding ones. Taken together, however, they cannot be very far from 20c. per pound as an average on all fluid extracts when made on a fairly large scale. If made upon the small scale of the dispensing pharmacist these elements would not be much greater if he had the intervals of time to devote to the work without greatly increasing his expenses.

But even if he used repercolation, and recovered his alcohol as well as is practicable on the small scale, the menstrua would cost him at least double the above estimates. Then he must buy his drugs by careful selection in the unground condition, because he could not be sure of the quality if ground, even though he might pay full prices. And in grinding them himself the loss and the cost would be greater. Therefore the net cost to him, as an average, could not well be less than one-third greater than in buying his fluid extracts ready made. But his intimate knowledge of the quality and character of his supplies far overbalances this additional cost and would fully entitle him to charge—not 33 p.c. more, but 100 p.c. more for what he makes than what he buys, and thus render them far more profitable to him. And he will get his prices easily, provided his general character be such as to inspire confidence in his ability and in the fidelity of his work.

The originator of the class of fluid extracts,—Prof. Wm. Proctor, Jr., of Philadelphia,—was not a manufacturer, but throughout his fruitful life was a dispensing pharmacist; and he earned first, by faithful ability,—and then commanded prices for his preparations which were liberally remunerative; but he never tried the experiment of putting on the profits and prices before he had earned them, and trusting to meretricious display for his results.

ASSAY OF JALAP.

The U. S. Pharmacopœia defines and describes jalap in its unpowdered commercial condition, and then gives the following test of quality.

"On exhausting 100 parts of jalap by alcohol, concentrating the tincture, and pouring it into water, a precipitate of resin should be obtained, which, after washing with water, and drying, should weigh not less than 12 parts, and of which not over 10 per cent. should be soluble in ether."

This test however cannot be applied to it in the commercial condition as described, because no two tubers are alike in medicinal properties, and no reasonable number of fractions could be taken from the tubers which in size and character would fairly represent any given parcel. Any one who has gone through the markets in buying, and has cut a dozen or more tubers from each bale in order to judge of the more or less resinous fracture of the pieces, will doubtless assent to the statement that the quality can only be indefinitely judged by former experience, and that lot will be bought which appears to be most resinous in fracture.

Jalap may also be usefully judged by its weight. Good Mexican jalap is found in bales of about 200 lbs. each, and those of smallest size in proportion to the weight are always the best jalap. Hence only the small bales need be opened for farther examination, because in the larger bales a greater proportion of pieces will be found of a light colored, starchy fracture, or be hollow.

Within the past few years the drug has fallen very much in price and different styles of packages are present in the markets, as though the drug was coming from different sources. Merchants are generally very reticent in regard to the sources of their importations, and are constantly on the alert for new sources of supply to put in competition with the old and thus reduce prices, or get a lead on low prices from new sources. It is however pretty well known that jalap is cultivated in several localities in the East Indies and in Jamaica, and from these conditions and the low prices, it may be reasonably inferred that the markets are now supplied from many different sources. But the yet more important fact seems to be that the quality is very much lower than formerly.

In 1867 the writer published a paper on Commercial Jalap (see Proceedings of The Amer. Pharm. Asso., 1867, p. 380, and Amer. Journ. Pharm., 1868, p. 65), in which is given the results of an experience of about six years. From this experience it was shown that the yield of resin varied between 11 and 16.25 p.c. and these results were in general accord with those published in other countries. Then, and for two or three years later, it was easy to select jalap that would yield 13 or 14 p.c. of resin.

After 1870, however, the quality began to fall off, and a carefully selected purchase for making the resin yielded only about 9 p.c. It was then found that the yield of extract had not diminished as much as the proportion of resin, and as the resin was the active portion, it became necessary in order to keep the officinal extract uniform, and up to the standard, to separate and exclude a portion of the inactive matters. And this practice of adjusting the extract to a uniform proportion of resin has been necessary ever since that time.

In the writer's experience of the past seventeen years jalap and all its preparations have gone very much out of use. In reviewing the usage for the purposes of this note, it appears that scarcely any powdered jalap is now called for, while the extract and resin have fallen off more than one-half from what they were for the ten years up to 1870. It was perhaps this falling off in the usage that influenced the Committee of Revision to drop the extract from the Pharmacopœia of 1880, leaving only the Abstract, the Compound Powder and the Resin as the officinal preparations. The alcoholic extract is, however, still used more largely than any other preparation, the resin being very little used.

Since 1875 no lot of jalap has been worked which yielded over 12 p.c. of resin, and from this the record runs down to one lot which yielded only 7.6 p.c., and all this jalap was carefully bought from this large market always well supplied.

The writer's attention was called to the subject some time since by Mr. W. L. Turner, a pharmacist of Philadelphia, who in examining many samples of powdered jalap from his market failed to find any that would meet the pharmacopœial requirement of 12 p.c. of resin. Some powder sent to Mr. Turner from the writer's stock also proved to be slightly (1 p.c.) below the requirement of 12 p c., and it therefore seems to be well to invite public attention to the subject and see whether the experience of other observers is in accord with Mr. Turner's investigations.

The process for assaying jalap as given by the Pharmacopœia, although as full as could well be given there, lacks many details which are essential to its successful application. It is very difficult to fully exhaust small quantities of a powder with any reasonable quantity of a menstruum by percolation. The writer has elsewhere shown that when 8 troy ounces of a fine powder are taken it cannot be practically exhausted with less than 7 or 8 times its weight of menstruum, and for complete exhaustion, by well-managed percolation, 10 times its weight is required. Smaller quantities are still more difficult to exhaust unless a Soxhlet apparatus or its equivalent be used. In the case of jalap powder the exhaustion by alcohol is not easily accomplished, and is not complete when the tincture fails to give turbidity on being dropped into water. As there are also some other steps in the management which require limitation, the following process is offered:

Put 10 grams. of finely powdered jalap on a tared watch glass and dry it for four hours at 100°C. and cool it under a bell glass before weighing. Jalap powder is very hygroscopic and varies much in the amount of moisture held in damp or dry weather. About 7 to 8 p.c. is the normal loss in drying from the commercial condition of powdered jalap, and should it lose more than this in drying the excess should be corrected for in the assay.

Into a flask of 250 c.c. capacity, put 25 grams. of finely powdered jalap and 75 c.c. of alcohol, shake well, heat to boiling, and then digest in a warm place for 24 hours with frequent shaking. Having arranged a pair of counterbalanced filters 15 c.m. or 6 inches in diameter, in a funnel and moistened them with alcohol, pour in the jalap magma and filter off the tincture into a vessel marked at 100 c.c. Rinse the flask into the filter with fresh alcohol, and percolate the residue on the filter with fresh alcohol dropped upon the edges of the filters and the surface of the powder until the filtrate measures 100 c.c. Transfer this filtrate to a capsule on a water-bath and start the evaporation. Return the contents of the filter to the flask by means of a spatula, add 25 c.c. of fresh alcohol and bring this to a boiling temperature in a water-bath ; shake well and again pour it into the filters. When drained again wash and percolate with fresh alcohol until another portion of 100 c.c. of filtrate is obtained to be evaporated with the first portion. Open the filters with the now exhausted residue, spread out the residue upon the upper one and place the whole to be dried at 100°C. or 212°F. When dry subtract the weight from the original weight of the powder, and the difference will be the weight of the extract and moisture taken out by the alcohol. This loss in weight varies with the quality of the jalap, from about 5 to 7 grams, or 20 to 30 p.c. Evaporate the total filtrate to the consistence of a thin extract, cool and add 10 c.c. of alcohol, stir well and add 10 c.c. of water, again stir and warm until a complete smooth mixture is made. Usually this makes a transparent solution, and if so more water should be added in small portions, with stirring until a permanent precipitate begins to form. Pour this into 125 c.c. of water in the original flask, and shake vigorously. Rinse the capsule two or three times, or until entirely clean, first with 2 c.c. of alcohol, and afterward with water, adding the rinsings to the contents of the flask. Shake vigorously and continuously until the soft resin precipitated adheres to the bottom and sides of the flask, and the watery solution becomes nearly or quite free from floating particles. Rarely it will be found that some of the precipitated resin remains suspended, forming a milky fluid. It must then be heated and shaken, and if still it does not separate pour it into a capsule and boil until it does, or until the water is nearly all boiled off. Then add cold water. Pour off the watery liquid into a pair of counterbalanced filters about 11 c.m., or 4½ inches in diameter. Rinse the adhering resin twice with 10 c.c. of water, and pass the rinsings through the filters last. The drained flask, cork and contents may then be weighed and the tare subtracted if the total weight of soft, moist resin be desired as an indication, or a check upon the final results. The filters containing the floating particles are dried at 100° C. and weighed, commonly giving not more than one or two centigrammes of resin. The filtrate should be entirely clear, and remain so on dilution with water. The contents of the flask are washed three times with 10 c.c. of stronger ether, by vigorous shaking, the successive washings being poured off into a tared capsule, evaporated and dried at 100°C., thus giving the approximate weight* of the ether soluble resin. The active resin remaining in the flask is dissolved by shaking with 10 c.c. of alcohol and the solution poured into a tared capsule. The flask and cork are then rinsed clean with 10 or 15 c.c. more alcohol, applied in small portions at a time, and the rinsings added to the solution in the capsule. The alcohol is then evaporated off at 100°C. and finally the resin is melted over a lamp, cooled and weighed.

The results are then as follows,—given from an actual assay:

First, the amount of accidental, or hygroscopic moisture in the powder by difference in weight after drying at 100° C.—.82 gram..........	=	8.20 p.c.
Second, the total dry extract by difference in weight of the powder before and after exhaustion,—25 grams. taken, less 8.2 p.c. of moisture, equal 22.95 of dry powder, less 19.25 grams., the weight of the dry exhausted powder or residue, leaves 3.70 grams. of total dry extract from the 25 grams., and this multiplied by 4 gives the percentage of this extract		14.80 p.c.
Third, the weight of soft, moist resin adhering to the flask in a wet condition,—2.71 grams., multiplied by 4.........................		10.84 p.c.
Fourth, the weight of the small quantity of resin caught by the small filters,—.012 gram., multiplied by 4		.048 p.c.

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* The washing with ether in this way does not take out all the ether soluble residue because the ether does not get access to the whole of the resin. But if very thoroughly shaken the results are sufficiently close.

Fifth, the weight of the portion of resin soluble in ether,—.2227 gram., multiplied by 4........ .89 p.c.

Sixth, the weight of the active portion of the resin,—1.595 grams., multiplied by 4 ... ... 6.38 p. c.

The last three items together give the actual amount of resin obtained from the powder,—7.32 p.c. According to the Pharmacopœia not more than 10 p.c. of this should be soluble in ether,—or .73 p.c., but instead of this .89 p.c. is ether soluble.

In ordinary practice, the moisture in the powder,—the total dry extract by difference,—the soft moist extract, and even the small amount caught by filtering the watery liquid,—may be neglected, and only the weights of the two resins be obtained, but this does not shorten the process much, since all the steps except the drying of the powder, the drying of the exhausted residue of the powder, and the filtration of the water after precipitation, have to be gone through.

Mr. Turner having found the tests of the jalap accessible in the Philadelphia market to be very low, and none up to the lower limit of the Pharmacopœia, and the writer having unexpectedly found his stock of powder to be but little better, it was decided to try what condition the powdered jalap of the New York market was in.

Half a pound of powdered jalap was bought from each of the seven largest and best wholesale drug houses in the city and these samples were assayed by the above process with the following results :

Sample Number.	Loss by Drying at 100°C. p. c.	Total Dry Extract by difference, p. c.	Moist Soft Resin, p. c.	Dry Resin on Filter, p. c.	Ether Soluble Resin p. c.	Active Resin p. c.	Total Resin, p. c.
1....	8.20	14.80	10.84	.05	.89	6.38	7.32
2....	8.49	16.23	16.00	.14	.74	8.22	9.10
3....	8.00	14.40	13.64	.06	.86	7.80	8.72
4. ..	8.43	19.56	.....	.13	1.19	6.50	7.82
5....	8.42	20.28	.....	.06	.95	5.50	6.51
6....	....	.....	.....	.33	.45	8.00	8.79
7....	8.40	18.62	.....	.04	.80	5.34	6.19
8....	6.30	31.38	31.56	.18	1.24	17.08	18.50
9....	10.00	20.96	....	.09	.71	7.60	8.40
10....	9.4	19.92	.....	.09	.40	6.24	6.73

No. 7 is a sample from a lot of 5 or 6 tons of jalap, which has a fine appearance and breaks with a good fracture.

The specimen No. 8 was obtained from a manufacturer who had bought a lot of unusually good jalap five or six years ago and had kept it ever since for making the resin of jalap.

The writer's experience of late years with jalap for making the extract and resin is as follows:

In 1879, a lot of 125 lbs. of powdered jalap gave about 17. p.c. resin.
“ 1882, “ 220 “ “ “ “ 13.4 “ “
“ 1883, “ 107 “ “ “ “ 7.6 “ “
“ 1885, “ 100 “ “ “ “ 7.9 “ “
“ 1888, “ 250 “ “ “ present stock, gives about 15.6 p.c. resin.

It is believed that at the present time there is not a bale of jalap in this market in wholesale hands that will yield 12 p.c. of officinal resin.

Nos. 9 and 10 are from the London market and represent two lots of the best Mexican jalap to be found there. From these it will be seen that the London market is in the same condition as this. In fracture and general appearance these two samples were unexceptionable.

EXTRACTION OF COCAINE.

Increased experience and observation in the extraction of cocaine led some months ago to a modification of the process which has been found to be a very considerable improvement.

The exhaustion by dilute sulphuric acid has been abandoned, and for the acid water kerosene has been substituted with the effect of quite as complete exhaustion with a saving of labor that overbalances the additional cost of kerosene over the acid water. The grade of kerosene used is that called in commerce “water-white, 150° test oil.” An oil of lower test, at lower cost would be used were it not that the increased risk from fire would overbalance the saving in cost.

Each 175 lbs. of the ground coca is moistened with an equal weight of a hot 10 p.c. solution of carbonate of sodium. To this is added, and intimately mixed, about 16 gallons or about 112 lbs. of the second kerosene percolate from a previous percolation. This powder, so moistened, is at once packed and percolated with the succession of weak kerosene percolates from a previous portion, and finally with fresh kerosene, to complete exhaustion, requiring in all about four to five times the weight of the cocoa of kerosene. The first strong percolate equal to the weight of the coca, is reserved for washing out, the other fractions of percolate going to the next portion of coca by repercolation, the loss of kerosene in the exhausted residue, and by subsequent rejection being about 25 p.c of the whole.

The strong reserved percolate is thoroughly agitated with about 6 p.c. of its weight of dilute sulphuric acid (5 parts acid s.g. 1.840 to 95 parts water), applied in two equal successive portions. The separation of the emulsions thus formed is facilitated by warming when, between the clear kerosene above and the solution of sulphate of cocaine below a thin stratum of fatty matter is found which has not been examined. This is carefully rejected, and the solution of sulphate is precipitated by carbonate of sodium in the presence of a small portion of warm kerosene, so that the oil is saturated with the alkaloid at a temperature of about 66° C. or 151° F. This warm solution is kept in a warm place and allowed to cool very slowly during 24 to 48 hours just to the point of commencing crystallization. During this time a dense, heavy, gummy matter separates and falls to the bottom of the vessel. The clear and nearly colorless solution is then poured off and crystallized by cold. The crystals are drained and pressed, and then redissolved in fresh kerosene to saturation at 66° C., again slowly cooled to the point of crystallization, when another very small portion of the gummy, sticky matter separates, and the now almost colorless solution is poured off from this, crystallized by cold, and again drained and pressed.* These gummy, sticky residues contain large quantities of cocoaine to be subsequently dissolved out by hot kerosene and crystallized. And, although repeatedly washed, no portion of this residue has ever yet been entirely freed from cocoaine. The quantity of crystals diminishes after many washings and finally a point is reached where the value of the time and labor exceeds the product, but much alkaloid still remains. This residue has never been investigated, but its behavior suggests that cocaine is really generated in it by the heating with kerosene. It can only be well managed when it has accumulated in considerable quantities.

The pressed crystals of colorless alkaloid are dissolved to saturation in dilute acid, the remaining kerosene separated, the solution washed with a little ether to separate the last traces of kerosene, and then precipitated by carbonate of sodium in the presence of fresh ether, s.g. .720. The clear ethereal solution of the pure alkaloid is finally shaken out with hydrochloric acid, and the solution of the hydrochlorate is evaporated to dryness as described at page 724, and in this condition it is put up and sold.

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* This crystallization is of late repeated a third time.

At page 986 the details of manufacture for 10 months were given up to Sept. 1, 1887. From that date to April 1, 1888, a period of 7 months, 286 bales of coca, yielding 43,262 lbs., were manufactured, the prices paid for the coca having varied between 19 and 35c. per lb. with an average cost of 24.45c per lb., giving a total cost of $10,452.45.

The estimated cost of manufacturing given at page 988, when corrected for some errors in the figures, was about 10.85c. per lb. of coca during 10 months practice. The cost during the 7 months just past has been much less, or only about 9.87 cents per pound of coca leaf, chiefly because the scale of operation was larger. Then 9.87 per lb. × 43,262 lbs. = $4,269.96 as the total cost of manufacture. Cost of coca $10,452.45 plus cost of extraction $4,269.96, gives $14,722.41 as the total cost for the 7 months.

From this it appears that by increasing the scale of operation about one-half, the cost of extraction is reduced by about 1c. per pound of coca,—or practically 10 p. c.

The proportionate yield of available salt has also increased, for while the preceding 10 months gave 22.05 grains of salt sold to the pound of coca bought, this 7 months gave 27.32 grains to the pound.

The actual average price realized for the 7 months sales was $6.36 per ounce, or 1.456c. per grain. Then 27.32 grains multiplied by 1.456c. gives 39.78c. realized for the product of each pound of coca, costing (24c+9.87=) 33.87c. Profit 5.91c. per pound, or about 17 p.c. on the average. The lowest price is in 50 ounce tins at $5.50 per ounce net, and the highest is in 5 grain vials at $7.87 per ounce net; the profit being only about 10 p.c. greater at the higher price, when labor and loss are carefully estimated. That is, the cost is proportionate to the size of packages, and the difference in actual cost is much greater than is generally supposed. For example, 87 five-grain vials are required for an ounce, with the corresponding corks, labels, wrappers, time, labor, and loss in weighing out.

IMPROVED PROCESS FOR ASSAYING COCA.

The improvement in the process of extraction just noticed was preceded by a similar improvement in the assay process, and now this latter is so simplified and so easy that it is well worth while to give it over again as now modified.

The so-called Truxillo coca always has a considerable but variable proportion of twigs and fruit which yield no alkaloid, and hence samples should be carefully drawn from every bale of each lot, and the mixed sample should be all ground and passed through a sieve of 30 meshes to the inch. In this grinding and sifting, the twigs and fruit go through last, and therefore the powder should be well mixed before the portion for assay is weighed off from it.

One hundred grammes of the ground coca is moistened thoroughly with 100 c.c. of a 7 p.c. solution of crystallized sodium carbonate, packed at once in a percolator, and percolated to about 700 c.c. of percolate, with kerosene.

On general principles it would not be supposed that the water-wet mass could be exhausted by percolation with an oil, and this proceeding was for a long time declined on this principle, but the exhaustion is nevertheless complete. Mr. C. M. Stillwell who, at the writer's suggestion, used this process, preferred to use the kerosene warm. But in critical trials of the same coca percolated cold and warm no difference was discoverable. Neither does more or less sodium carbonate change the result. The 700 c.c. of kerosene percolate holding all the alkaloid in solution, is transferred to a separator, which is not more than two-thirds filled by it, and 30 c.c. of a 2 p.c. hydrochloric acid is added, and the whole is well shaken together, but not so hard as to make an emulsion that will not separate in a half hour. The watery solution is drawn off from below into a smaller separator, and a fresh portion of 30 c.c. of the dilute acid is added to the oil,—shaken and separated as before. This washing of the oil with dilute acid is repeated a third time, when all the alkaloid will be in the small separator as an acid hydrochlorate. The next step is the final precipitation of the alkaloid in the presence of ether, by sodium carbonate, and in order to avoid a deficiency, or too great an excess of the sodium carbonate, a measured portion of fresh 2 p.c. acid is saturated with a weighed portion of the sodium carbonate, and the quantity required to precipitate the cocaine from the solution of acid hydrochlorate is calculated from the result of this saturation. The amount of sodium carbonate required, plus 5 p.c. for excess, is then weighed off for the precipitation. The acid solution in the small separator is then first well washed with 30 c.c. of strong ether to remove adhering oil and coloring matter, and the washing thrown away. Then 20 c.c. of fresh ether is added, and the sodium carbonate in small portions at a time to avoid loss by effervescence. The whole is well shaken, the watery solution drawn off from the ether into another separator, and the ethereal solution carefully transferred to a tared beaker. The watery solution is again twice washed with 20 c.c. of fresh ether each time,—the ether washings added to that in the beaker, and the watery solution, now free from alkaloid, is thrown away. The beaker with the ethereal solution is set in a warm place until the ether is evaporated, when the alkaloid is dried at 100° C., cooled and weighed. This weight expresses, of course, the percentage of cocaine obtained from the sample assayed.

After a little experience with this process two assays may be made in 24 hours, or say five or six within 48 hours. By the use of a filter pump for the percolation an assay can be easily made between morning and evening.

The following 26 lots of coca were assayed during February and March, with the results given. Total of bales, 324.

12	Bales	of Truxillo	.916	p. c.	2	Bales	Truxillo	.637	p. c.
20	"	"	.714	"	4	"	"	.647	"
32	"	"	.806	"	5	"	"	.706	"
6	"	"	.588	"	6	"	"	.852	"
6	"	"	.628	"	10	"	"	.716	"
36	"	Huanuco,	.571	"	54	"	Huanuco,	.747	"
24	"	Truxillo,	.753	"	2	"	Truxillo.	.560	"
20	"	"	.778	"	6	"	"	.839	"
6	"	"	.973	"	12	"	"	.777	"
2	"	"	.498	"	7	"	"	.795	"
6	"	"	.983	"	8	"	"	.755	"
2	"	"	.854	"	2	"	"	.662	"
6	"	"	.528	"	36	"	"	.338	"

In the applications of the chloroform reactions to discriminate between different specimens of hydrochlorate of cocaine an improved practice has been reached. At page 989 et seq., the importance is shown of using both the chloroform and the salt as free as practicable from alcohol and water. The improved practice with this test is to use only chloroform that has been recently shaken with strong sulphuric acid, and to dry the salt at 100°C., noting the loss by drying, and weighing the .4 gram from the dried salt. Taking these precautions it is now not uncommon to find salts so good as to require 10 to 12 c.c. of dry chloroform to dissolve the .4 gram. of dry salt, whilst a year ago none were found requiring over 7 to 8 c.c.

HYDROBROMATE OF QUININE.

This salt seems to have been introduced to therapeutic use chiefly, if not solely, as being well adapted to hypodermic use.

The administration of quinine hypodermically has always been so desirable that a great deal of ingenuity has been brought to bear upon getting a solution concentrated enough to bring the dose within the limited range for hypodermic use, and yet to have the concentrated solution as free as practicable from caustic or irritant qualities.

It may perhaps be accepted as a practical rule that a solution containing about one grain of the alkaloid, equal to one and three-tenths grains of the ordinary sulphate of quinine, in ten minims of solution, is the limit which is not too dilute for useful hypodermic application, and yet not too caustic by concentration. Any solution more dilute has too large a dose, and any that is more concentrated will too frequently produce abscess, especially when, as is commonly the case, the concentration is obtained by the use of free acid. Of all the salts proposed the hydrobromate has been the one which seemed best to meet these indications, the acid element being here the least irritating. Some such considerations seem to have led to its introduction into the last revision of the U. S. Pharmacopœia, where it appears as follows :

QUININÆ HYDROBROMAS.

HYDROBROMATE OF QUININE.

$C_{20}H_{24}N_2O_2HBr.2H_2O$; 440.8.–$(C_{20}H_{12}NO_2)_2,HBr.4HO$; 440.8

Hydrobromate of Quinine should be kept in well-stopped bottles.

Colorless, lustrous needles, permanent in ordinary air, but readily efflorescing at a gentle heat, odorless, having a very bitter taste, and a neutral or slightly alkaline reaction. Soluble in about 16 parts of water, and in 3 parts of alcohol at 15° C. (59° F.) ; in 1 part of boiling water, and in less than 1 part of boiling alcohol ; in 6 parts of ether, in 12 parts of chloroform, and moderately soluble in glycerin. On ignition, the salt burns slowly without leaving a residue. The aqueous solution, when acidulated with sulphuric acid, has a blue fluorescence, and, when treated, first, with fresh chlorine water, and then with a slight excess of water of ammonia, it produces an emerald-green color. Water of ammonia added to the aqueous solution throws down a white precipitate readily soluble in an excess of water of ammonia, or in ether. Test-solution of nitrate of silver produces a white precipitate, which is insoluble in diluted nitric acid, and, when filtered off and washed, insoluble in solution of carbonate of ammonium.

The salt should not be colored, or not more than very slightly colored, by undiluted sulphuric acid (abs. of foreign organic matters), nor be reddened by nitric acid (difference from morphine). If a small portion of the salt be dried on the water-bath until it ceases to lose weight, and the residue cooled in a desiccator, the loss of weight should not exceed 8.2 per cent. The aqueous solution should not be rendered turbid by diluted sulphuric acid (abs. of barium), and not more than slightly turbid by test solution of chloride of barium (limit of sulphate). If 1.5 Gm. of the salt be dissolved in 15 C.c. of hot distilled water, the solution stirred with 0 6 Gm. of crystallized sulphate of sodium in powder, the mixture maintained at 15° C. (59° F.) for half an hour and then drained through a filter only large enough to contain it, until 5 C.c. of filtrate are obtained—upon treating this liquid as directed for the corresponding test under quinine (see *Quinina*) the results there given should be obtained.

The salt here defined by the formulas is the neutral salt, but the description does not apply to this salt, nor to any other that can be found or made in regard to the all-important point of solubility in water. It is described as being soluble in 16 parts of water, but is really soluble only in about 53 parts.

This market is supplied with the officinal salt by two manufacturers, but all attempts to get it to dissolve in the described proportion of water have failed, and always will fail, and this fact frequently brought to the writer's notice led to this investigation of the subject, all attempts by physicians to use this salt hypodermically having failed. One part of the officinal salt in 16 parts of water require the addition of 1.25 parts of diluted (10 p.c.) hydrobromic acid for complete solution at 15° C. (59° F.), and the solution is then a mixture of neutral and acid salts ; and being 1 in 16 instead of 1 in 10, it is not well adapted to hypodermic use. Hence the Pharmacopœia is in error, either as to the salt defined or the salt described, and if the error be in the definition it cannot be corrected so as to agree with the description, because there is no such salt. And if there was such a salt, its saturated solution would be too dilute for hypodermic use.

A salt of foreign make was found in this market, at a high price, which is adapted, and is used for hypodermic solution, but this is labelled dihydrobromate of quinine, being really an acid hydrobromate; and this is probably what the Pharmacopœia intended, —or at least what it should have had. This is a true, crystalline salt, consisting of 2 molecules of hydrobromic acid and 1 molecule of quinine. Its percentage composition is:

		That of the neutral salt	
Quinine	60.04 p.c.	is Quinine	73.50 p.c.
Hydrobromic acid	29.95	Hydrobromic acid	18.33 p.c.
Water	10.01	Water	8.17
	100.00		100.00

The acid salt is soluble in about 6 parts of water, and the neutral salt in about 53 parts, and there appears to be no salt between them. Although different authorities differ in giving the composition of these two salts, and call them by different names, yet no third or intermediate salt has been described so far as the writer could discover, and all efforts to make any other by any of the processes given, have failed.

In the *Year Book of Pharmacy* for 1875, p. 52, is an abstract from *Journ. de Pharm. et de Chim.*, xx., 181, wherein M. Boille presented to the French Academy of Medicine an account of a salt which he calls Neutral Hydrobromate of Quinia, with a percentage composition as follows:

Quinine, by experience	75.20	by theory	76.59
Hydrobromic acid "	18.26	" "	18.91
Water "	4.80	" "	4.25
	96.26		99.75

This salt is described as being soluble in five times its weight of water. The process given for making it is by simple combination of hydrate of quinine with dilute hydrobromic acid, but all efforts to get anything but the two above-mentioned salts, the one soluble in 6, the other in 53 parts water, by this process, also failed.

Under the Pharmacopœia caption or title, both the Dispensatories (U. S. and National) give processes for making the hydrobromate, but none of these could be made to yield anything but the acid or neutral salts, or anything that would anywhere nearly accord with the Pharmacopœia description.

In examining all the authorities within the writer's reach, nothing was discovered that would account for, or lead to the discrepancy between the definition and description of the Pharmacopœia, or to account for the reason of both being wrong, and had the salt been much used these errors must have been heard from long ago.

The salt needed for hypodermic use, namely, the acid salt, is very easily made by simple direct combination between the acid and base, and is easily crystallized and dried without decomposition, and it is probably quite as permanent as any of the acid salts of quinine. It contains just about the same proportion of quinine as the bisulphate, but the acid element is less irritant. The acid sulphate is soluble in 10 parts of water, the acid hydrobromate in 6, and the saturated solutions seem to be both liable to produce abscess, though the acid hydrobromate is less liable than the acid sulphate. The small quantity of the bromine element in any hypodermic dose can have but little therapeutic effect, but what it has tends to correct quininism. When, however, large doses are required, as in pernicious intermittents, for example, the bromine element becomes effective for good.

In all cases where neither the stomach nor rectum will accept the quinine, and when the oleate applied to the skin is too slowly absorbed, the hypodermic use of it becomes very important, and then no salt is equal to the acid hydrobromate.

IODIDE OF ETHYL.

Ethyl-Iodide is a substance well adapted to a few uses in the materia medica, and some of these uses appear to be important. But the occasions for employing it being rare, and the liquid being difficult to preserve in good condition for use, and when needed being generally found in a bad condition, or to have been badly made,—all these circumstances seem to have conspired to keep it in the background, comparatively inaccessible and forgotten. Thus it might be useful to try to devise some means of keeping it in a good condition, with a view to affording it in such condition.

It is a colorless, volatile, very heavy liquid, of an agreeable ethereal odor, composed of one molecule each of ethyl ($C_2H_5=29$) and of iodine ($I=126.6$). The s.g. at 15.6°C. compared with water at the same temperature is 1.9428,—boiling point about 79°C. or 175° F. Mendelijeff gives the s.g. at 15°C. as 1.9309, but this is probably compared with water at 4°C. Andrews gives the boiling point as 71.3°C.

It is colorless only when it has not been exposed to light, as even a very slight exposure gives a reddish-brown tint from decomposition by which iodine is set free. But a very slight degree of decomposition gives a very considerable depth of tint, so that when the color does not exceed a wine color it may be disregarded in use. And even when deeper than this the free iodine which evaporates with the liquid is not in sufficient quantity to produce irritation. The product of the following process, to which product the above given description applies, has a disagreeable alliacious odor in slight degree, which is supposed to come from the presence of arsenic in the phosphorus,—and no phosphorus is accessible that is free from arsenic. If the odor be from arsenic, however, the quantity is too small to be discovered by the ordinary tests.

The best process for preparing iodide of ethyl for medicinal uses seems to be that of Beilstein and Rieth as quoted by Roscoe and Schorlemmer, Vol. III., Pt. I., p. 347, from *Ann. Chem. Pharm.* CXXVI., 250, very slightly modified as follows:

Iodine, resublimed, of commerce	1,000	parts or grammes.
Alcohol, clean, s.g. .814 to .820	500	" " "
Amorphous Phosphorus	100	" " "

Grammes are used in this process, and the alcohol and phosphorus are weighed into a flask of about 2 litres capacity. The flask being set in a large basin of cold water, the iodine is added in portions of 100 grammes at intervals of about 15 minutes, the contents being well shaken round about 10 minutes after each addition of iodine and again just before the succeeding addition. By this management the contents become very warm, but not very hot. When the iodine is all added the flask is loosely stopped and set aside for 24 or 48 hours. The flask should be now managed and handled very cautiously, since from the great weight of the liquid the slightest touch against any hard object breaks it.

The flask is then fitted up for distillation in a salt-water or dilute glycerin bath, using a Liebig's condenser with glass tube, and distilled until the rate is reduced to slow dropping. The weight of the distillate is 1230 to 1240 grammes. The residue in the flask may be thrown away or may be used for making phosphoric acid. The distillate is highly colored by free iodine. It is transferred to a separator and shaken with a very diluted solution of soda until it is quite free from color. This decoloration is usually accomplished by 30 c.c. of normal test solution of soda in 100 c.c. of distilled water;

but if the decoloration be not complete 10 c.c. more of the test solution will complete it. The liquid is then separated from the washings into the cleaned and dried flask, and is then rectified in the same way that it was first distilled. The first 100 c.c. of distillate will contain most of the water that was dissolved, and will be cloudy from the presence of this. It is convenient to receive this fraction separately in a small flask filled to half-way up the neck. Then in about 12 hours' standing the water will separate and may be taken from the top by bibulous paper, and the clear liquid below it be added to the remainder of the rectified distillate. This first fraction of the distillate sometimes has a much more marked garlicky odor than the larger portion, and if so, it is poured into a capsule and heated slightly until it is freed from the excess of this odor, and this heating may entail a loss of 30 to 50 grammes. When this loss is not necessary the total yield will be about 1120 to 1130 grammes,—or when the loss is necessary, about 1080 grammes. The product should be at once put up in small vials, and for economy in dispensing for use these should not contain more than an ounce, because a portion of each vial will be spoiled before it is all used, even with good management. An ordinary half ounce vial, cork stopped, is the proper container for an avoirdupois ounce, and as this measures just 15 c.c., it may conveniently be put up by this measure. As a partial, but useful protection against discoloration by keeping, —although it does not at all prevent the decomposition which causes the liquid to become colored, but merely saturates the iodine as it is set free,—it is advisable to put upon the surface of the liquid in each ounce vial 5 c.c. of a solution of soda made by mixing 20 c.c. of normal test solution of soda with 80 c.c. of water. Without this, even with great care to exclude light, the ether will in a month or two become distinctly brown tinted, and in 6 months to a year will be of a pale wine color. When not deeper than this it is entirely fit for use; and when much deeper it can be easily decolorized by shaking with a fresh portion of dilute soda solution.

It is very important to state that from beginning to end this process should be, or rather must be conducted by artificial light of low intensity. In the putting together of the elements, and during the first distillation the exclusion of light is not essential, but for the rectification and putting up, light should be excluded,—and no daylight should get access to the vials until after they are wrapped in dark, thick paper. Even with such wrappers the vials should be kept in a cool, dark place.

When in use by nurses or patients the wrappers should be kept on, and be only loosened around the cork and the lip, and the vial should be kept in the dark.

It is used by inhalation only, and the best way to administer it is to drop the dose into a small wide mouth vial and inhale the vapor directly from the mouth of the vial through the nostrils, using the warmth of the hand around the vial to hasten the evaporation. Inhaling the dose from an handkerchief is a very wasteful and uncertain mode of administration, and although generally recommended it is not the best way nor a good way.

The dose to begin with is 15 to 20 drops, but when indicated at all it should be pushed to some distinct effect before being abandoned, and then if useful the effective or useful quantity will be ascertained, and may be repeated several times a day.

Iodide of ethyl under the name of hydriodic ether seems to have been introduced to therapeutic use by Dr. Huette in a paper published in the *Journal de Pharmacie* for October, 1850, and an abstract of this paper, and of another by M. Cap, is given in *The Amer. Jour. of Pharmacy,* 1851, Vol. 3, or New Series xvii., p. 154. In *The Medical Record,* 1880, Vol. 17, p. 688, is a paper by Dr. Robert M. Lawrence of Boston, on The Therapeutic value of Iodide of Ethyl, wherein may be found a good bibliography of the subject supplemented by Dr. Lawrence's experiences.

It is the easiest, most convenient and most rapid means known for saturating the organism with iodine. Iodine is found in the urine within a quarter of an hour after from 15 to 18 inhalations of the vapor, and continues to be so found for 60 hours, (Huette). Hence as an adjunct to iodide of potassium when this is required in large quantities as in syphiloma and other conditions of secondary and tertiary syphilis, it is well adapted to be useful. It does not weaken the digestive organs nor impair the appetite as large doses of iodide of potassium often do when they have to be continued to saturation, but has a rather stimulant, tonic effect. (Huette and Germain Sée.) With such considerations as guides to its general use it has been successfully applied in many neuroses of the respiratory and circulatory apparatus,—to chronic capillary bronchitis,—to many forms of asthma, and to the temporary relief of dyspnœa from whatever cause.

Those who use it should remember that it is about four-fifths iodine, and that the inspiration of 15 to 20 drops from a wide mouth vial will probably result in the absorption of say one-fourth of it, – or 4 to 5 drops, weighing 6 to 7 grains. Four-fifths of this, or say 4 to 5 grains would be iodine. Any such dose of free iodine would be so irritant as to be poisonous, the usual dose of free iodine, as in the Compound Solution (Lugol's Solution) being ¼ to ½ grain. Iodide of potassium, however, is over three-fourths iodine, and 10 grains of this salt would therefore represent about 7.5 grains of iodine.

As iodine is much less irritant when combined with a base than when free, and is equally effective, it is generally used in combination with some base. Then as the base ethyl of the salt iodide of ethyl is less irritant, (or rather is not at all irritant under any known circumstances)—than the base potassium of the salt iodide of potassium, and as iodide of ethyl is much more easily resolved into its elements than iodide of potassium, it follows that the former salt has at least these advantages over the latter in rational therapeutic uses.

OPIUM ASSAY.

The subject of the determination of the proportion of morphine in opium is everywhere attracting more attention than ever before, and it is very fortunate that several able investigators are giving much time and attention to it. Since the last note in these pamphlets, see page 965, many papers have been published, adding much to the knowledge of the subject, and it is here proposed very briefly to review two of the most prominent of these.

In *The Chemical News*, London, of March 9th and 16th, 1888, is an elaborate paper "On the determination of the amount of Morphia Present in Opium, by E. F. Teschemacher and J. Denham Smith." This paper is, in the main, a pretty severe criticism and condemnation of all the more modern work on the subject, bringing its heaviest strictures to bear upon the process of Prof. Fluckiger as modified by the writer, and the same process as modified by Mr. C. M. Stillwell, of New York. After a great deal of adverse criticism and ridicule of these two processes, and after passing over many others more leniently, it is a great surprise to find that the process of Messrs. Teschemacher and Smith, shown to be the only one deserving of confidence, is practically identical with that of Mr. Stillwell, the chief difference being in the use of benzene by Messrs. T. and S. for the purification of the crude morphine, instead of alcohol as used by Mr. Stillwell. Messrs. T. and S. check their final results by titrating the morphine with standard hydrochloric acid, while other operators have done this long ago with normal solution of oxalic acid, which is to be preferred on account of its easy preparation. The most conclusive answer to these severe strictures that can be offered is found in the following circumstances:

The heavy dealers in opium care little for processes of assay, but do care very much for a moderate degree of accuracy in results, and will go to any moderate amount of trouble and expense to satisfy themselves in regard to these results. Messrs. T. and S are well known and trustworthy assayers of opium in the London market, while Mr. Stillwell and the writer are fairly well known in this market. Repeatedly within the past five years shipments of opium have been bought in the London market on the assays of Messrs T. and S., and on arrival here have been sampled and assayed by Mr. Stillwell and by the writer independently,—the owners of the opium only, knowing of the independent assays until long after they were made. As a rule these three independent assays agreed within the limit of three or fourth-tenths of a per cent. or quite as closely as the conditions under which they were made would admit,—that is, the sampling at different times of the same lot of opium by different persons. In these trials sometimes one and sometimes another would be higher. Within the past six months, however, a much more critical trial was made by an importing house of this market. A large sample of opium was drawn and mixed to complete uniformity. It was then divided in three parts, each part wrapped in tinfoil, and one sent to each of the three assayers named without permitting either to know that the other samples were being assayed by others. The final results were within three-tenths of one per cent., Mr. Stillwell being highest, Messrs. T. and S. second, and the writer lowest, —all being satisfactory to the house who paid for the assays, and as near as they expected or desired to come, because they were convinced that under the conditions of the problem of opium assaying closer results are not practicable.

Upon this the writer wishes to give emphasis to what he has again and again written, namely, that refinements of this process of assay which limit its use to the hands and laboratories of professional experts, and by which only two or three-tenths of a per cent. in accuracy is gained,—are not desirable excepting in rare cases of disputed sales. And that a process that can be applied with a moderate degree of accuracy, by the largest number of persons in interest, is seriously injured by the refinements of special expert skill. When opiums of the markets vary all the way between 7 and 16 per cent. in morphine value, a process of assay which will discriminate between two samples to within a half of one per cent. and can be applied by pharmacists and physicians in general, will be of more value to the whole interest involved than a process which reaches greater accuracy, but can only be applied by a very few special experts.

Regarding the use of the word "assay" as applied to the opium process, Messrs. T. and S. say to Mr. Allen, "Do not let us Englishmen corrupt our own language." English dictionaries if followed back will lead most persons to the conclusion that assay is good usage, and properly applied when but one or two elements of a complex substance are to be estimated or valued.* Analysis signifies that the substance is separated into all its component parts, each part to be recognized in qualitative analysis; but in quantitative analysis each part is to be weighed or the proportions known. In assaying, whether it be an ore for the proportion of iron it contains, or opium for the proportion of morphine, assay—and not analysis,—is the proper word. Differentiation of ideas make such distinctions not only useful but necessary.

Finally at the end of their paper Messrs. T. and S. state that even if the U. S. Custom House examiners have the capacity to examine opium, they "have no method whereby they could determine whether or no an opium does contain 9 per cent. of morphia; so that they cannot fulfill their instructions, but simply act according to their will and pleasure."

This is a great mistake, for it is within the knowledge of the writer that these examiners use practically the same process that is claimed by Messrs. T. and S. as theirs, and it may be found in The Journal of the Amer. Chem. Society for 1885, vol. vii., p. 45, under the caption "Estimation of Morphine in Opium, by J. Howard Wainwright, Ph. B.,"—Mr. Wainwright being one of the chemical examiners of the U. S. Custom House at New York.

By favor of Dr. Wm. K. Newton, the State Dairy Commissioner of New Jersey, the writer has received that part of his report which embraces the estimation of morphine in opium for the purposes of the State law on adulteration. The Commissioner's experience having led him to conclude that the methods of assay were unsatisfactory, he placed the subject in the hands of Henry P. Cornwall, Professor of Analytical Chemistry in The College of New Jersey at Princeton, and Prof. Cornwall has made an elaborate report, which, from his well-known ability, is entitled to very great weight, especially as each reported result was checked by a duplicate assay by his assistant, L. W. McCoy, Sc.D.

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* To assay was originally to try. See Richardson, "She assayed in vain to speak;" "I will assay you; draw and defend yourself." To try any personal quality,—or try one's metal naturally came to trying the metal in a compound or in an ore,—that is, trying it or assaying it for one or more of its elements, but not for all, as in analysis.

He applies and reviews Prof. Fluckiger's process as modified by the writer,—and as modified by Mr. C. M. Stillwell,—the process of the U. S. Pharmacopœia,—Dieterich's process. (Eugene Dietrich in the *Pharmaceutische Centralhalle*, xxvii., 529 and 541)—the same process modified by himself,—and Kremel's method (A Kremel, *Pharmaceutische Rundschau*, v. 283, from *Pharm. Post*, 1887, 20, 661, and the *Chem. Zeit.*, 1887, 258,)—and he reaches the following conclusions:

Prof. Fluckiger's method as modified by E. R. Squibb, owing to the limited washing, is liable to give too high results.

Stillwell's modification of the last modification provides the means of arriving with certainty at correct results, with opium of any grade.

The U. S. Pharm. method, while open to theoretical objections, appears to be well adapted to opium of average quality, if very carefully executed; it is less liable to error in the case of officinal extracts and tinctures of opium than with opium itself.

Dieterich's methods, as improved by himself, are accurate for officinal extracts and tinctures, but still too low in the case of opium.

Dieterich's method, with the complete extraction finally adopted by Prof. Cornwall, gives accurate results for opium, and is the method least liable to error in comparatively unskilled hands.

Kremel's method gives too low results for opium, and is in any case inferior to Dieterich's, both as to accuracy and convenience.

These conclusions will bear the following criticisms. They were all reached from one single specimen of powdered opium which when dried at 100° C. contained 13.3 p.c. of morphine. In Anatolia there are over 20 districts yielding opium to the markets, and the product of each differs somewhat in its reaction with different processes;—while Macedonian opiums, which are about the best known, are again quite different in their structure or physical constitution. Literally, then, and for great accuracy,—that is for the expert chemist,—the best method for one opium would not be the best for others, because it is very well known that all the principal constituents of opiums of the markets vary quite as much in proportion as the morphine, yet do not vary in the same ratio with the morphine or with any other single constituent. From this it follows that the best process of assay might not be that best adapted to any single sample of opium, but rather that which is most generally applicable to different samples, and in hands not specially trained to analytical work, but simply capable of making assays with a moderate degree of accuracy. This is all that has ever been claimed for the writer's modification of Prof. Fluckiger's process, and in a large number of instances, with opium from different sources, the results of this method have been checked by other methods, and by actual experience on a large scale, without having been found too high. And farther, the method has been frequently compared with Mr. Stillwell's modification of it, by parallel assays in different hands of about equal capacity, and with different opiums as they come along in the market, and yet without greater differences in result than those inseparable from the conditions of such an assay process. That Mr. Stillwell's modifications are very valuable, and give much confidence and support to the accuracy of the results, is at once fully admitted, and the writer heartily joins in Prof. Cornwall's statement that they provide a means of arriving with certainty at correct results. But the question is simply, are they necessary in every day practice for commercial purposes,—and do they not endanger the results, when in ordinary inexpert hands, rather than improve their accuracy?

In regard to the method of the U. S. Pharmacopœia, Prof. Cornwall is the only writer now called to mind who has been able to make that process yield as well as he does, and therefore his testimony is very important upon this point. The general testimony is that its results are too low by about .8 to 2 p.c. and in view of this new evidence it would be well worth while, if not quite necessary, that the writer and others should again go over their work upon this process to see if they were in error, and to judge of the reasons lately given why it cannot be trustworthy. Two or more writers have shown that no ordinary lime process can be trustworthy, because every degree of excess of lime increases the degree of solubility of the precipitated morphine in the mother-liquor, and morphine so held escapes being weighed in the result.

If so high a degree of expert skill be employed as to adjust the proportion of lime to each opium tested, so as to always avoid any excess, then this objection to the method would fall, but would still leave others which are quite important, such as the taking of an aliquot part,—the precipitation from so large an amount of solution, by the use of so large an amount of chloride of ammonium by which the morphine is rendered more soluble in the mother-liquor,—and the failure to ascertain the purity of the precipitated morphine.

To these Prof. Cornwall adds that the results vary considerably with the degree of pressure of the crystals between the sheets of bibulous paper, as directed.

Dieterich's and Kremel's methods have never been applied by the writer, first for want of confidence in his ability to apply them properly and accurately, and next for want of confidence in some of the details which are common to other processes and which have been unsuccessfully tried.

The practical accuracy or inaccuracy of the U.S.P. process of assay is constantly assuming greater importance as the laws of the different States, one after another, are making the U.S.P. their legal standard for all medicinal substances.

So far as known every State law which adopts a standard at all adopts the U.S.P., and this, of course, includes the standard for opium. This officinal standard for opium requires that in its normal moist condition it should *yield* not less than 9 p.c. of morphine, when assayed by the officinal method given. And under powdered opium it requires that the powder should *contain* not less than 12 nor more than 16 p.c. of morphine when assayed by the process given under opium.

In order that a 9 p.c. moist opium should yield a 12 p.c. powder, it must lose 25 p.c. of moisture in drying. But as opium very rarely contains this proportion of moisture, and as the average is not above 20 p.c., and as a 9 p.c. opium with 20 p.c. moisture yields a powder of only 11.25 p.c., the Pharmacopœia is inconsistent within itself and cannot be applied as a standard within its own limit of error.

But it is rather against its process of assay that the grave objection lies. It has been repeatedly claimed and shown by the writer and others that this process in any ordinary hands does not yield all the morphine that opium contains, and that different varieties of opium from Asia Minor contain from 1 to 2 p.c. more morphine than is yielded by this process; and therefore that an opium to *yield* 9 p.c. by this process must really *contain* from 10 to 12 p.c.

The principal objections to this process are first, that it is applied to a proportion of the opium taken for assay which may or may not be an aliquot part of the whole, but which is generally less than it is assumed to be. Second, that an excess of lime is directed, while any excess diminishes the amount of morphine precipitated by rendering it soluble in the mother-liquor in proportion to the excess. And that lime is inadmissible to any process of opium assay because it cannot be easily adjusted in quantity so as to avoid excess or deficiency. Third, that the precipitation from so dilute a solution involves the loss to the assay of all the morphine which the solution will hold at the point of saturation. Fourth, that the chloride of ammonium is directed in excess, and thus adds to the capacity of the mother-liquor to hold morphine in solution. Fifth, that there is no testing for purity of the precipitated morphine directed,—and finally, that all these defects, excepting the last, are in the direction of too low a result, and the lowness of result will vary with the degrees of these defects as they apply to different specimens of opium, the observed limit of error being very rarely less than 1 p.c. or more than 2 p.c.

In view of Prof. Cornwall's very successful results with this process it has now been again gone over by the writer and a practiced assistant with much care and accuracy.

A case of Constantinople opium was carefully sampled, a large sample being taken and very thoroughly mixed to a condition as nearly homogeneous as possible. Eight portions were weighed off for assay, and four were independently assayed by each person. Each assayed one portion by Mr. Stillwell's method of washing with morphiated solutions,—one by the writer's modification of Prof. Fluckiger's method, as given at p. 965, and one by the U.S.P. method. One of the remaining assays was by the writer's method, for confirmation, and the other by the U.S.P. method, excepting that 2 grams. each of the recently slaked lime and chloride of ammonium were used instead of 3 grams. as directed. In all three applications of the U.S.P. process the quicklime was slaked with half its weight of water, instead of one-third its weight, as is more common.

The results of these assays are as follows :

Stillwell's method in two different hands,	14.29 p. c.	14.24 p. c.
E. R. S.'s method " " "	14.16 "	14.20 "
U. S. P. " " " "	12.72 "	12.52 "[*]
U. S. P. " with less lime and $N.H_4Cl$.	12.71[†]	
Triplicate of E. R. S's. method		14.32 "
The average of the 5 assays by two processes is......		14 242 p. c.
" " 3 " " U. S. P. process is...		12.650 "
Difference		1.592 "

Only 3 of the insoluble, exhausted residues of the assays were dried at 100° C. and weighed, and these gave 28.72,—28,42, and 28.27 p.c. of the original opium.

Two portions of the mass were also dried at 100°C., giving a loss of moisture of 18.24 and 18.44 p.c.

These slight differences in the residues and in drying under exactly the same conditions indicate the want of complete homogeniety in the sample mass,—a condition that can, of course, only be approximated.

If the above given results can be trusted,—and similar results have been seen often enough by the writer to be trustworthy to him,—the application of the U.S.P. process fully sustains the rational objections against it. Therefore neither that nor any other lime process is applicable to assaying opium.

Now, whenever these three processes are applied to the same opium there will be an average difference of abont the amount indicated, and this want of agreement has already caused much trouble under the laws of those States which have made the U.S.P. their legal standard, and the difficulty will be sure to get into the Courts if the State Examiners undertake prosecutions based upon the U.S.P. authority, whilst the General Government in its Custom Houses adopts a better method of assaying.

Dr. Bennett F. Davenport, the enegetic Examiner under the laws of Massachusetts, publishes in *The Druggists' Circular* for March, 1888, p. 52, a correspondence with the Treasury Department in which he makes a general claim that the U.S. law having adopted the U.S.P. as a standard of strength and purity, the opium admitted into the country through the Custom Houses should be governed by the U.S.P. process of assay, and asks that the method now in use be replaced by the U.S.P. process, so that the discrepant results as above shown may be avoided.

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[*] When this morphine was tested by solubility in lime water a very considerable proportion of it was found to be insoluble, and this should be weighed and deducted as in the other processes.

[†] The lime and chloride of ammonium were found to be still in excess in this assay.

This the Secretary of the Treasury, Mr. C. S. Fairchild, declines to do and gives his reasons, but as he does not go into the history and details of the matter, Dr. Davenport thinks,—and Prof. Cornwall will be likely to agree with him,—that the Department is wrong and uses its authority in the matter arbitrarily. But Dr. Davenport does not go over the entire ground in the matter, and his partial view fails to show him that the Secretary, however disposed, could not lawfully do what he asks.

In response to a general agitation on the subject of the importation of adulterated and spurious drugs and medicines, the Congress on June 26, 1848, passed a law, Chapter LXX., Statutes at Large IX, p. 237, governing such importations. This law permits the importation of drugs, medicines, etc., which are not "inferior in strength and purity to the standard established by the United States, Edinburgh, London, French and German pharmacopœias and dispensatories,"—and by this law, says Dr. Davenport, the Treasury Department is bound to apply the standard established by the United States Pharmacopœia.

Under this law of 1848 the Department established a set of Regulations for its enforcement, among which is found one directing that opium containing less than 9 p.c. of morphine shall not be admitted into the United States. This Regulation had the full force of law, and has now governed the practice and policy for 40 years. In 1883, however, this Regulation became a law by Act of March 3d. Hence, if prior to 1883 the Secretary of the Treasury had the power to modify a Regulation, he since 1883 has lost that power by the Regulation having become a Statute.

As a Regulation, however, it had all the force of a law. Just when the Regulation was issued does not appear, but the U.S.P. revised in 1850, two years after the law was passed, has no standard of strength for opium, and therefore disregarded the law or the Regulation made upon it.

At the revision of the Pharmacopœia for 1860,—the 9 p.c. law having been in force ten or more years, and the Pharmacopœia up to this time having had no standard for opium,—the writer, serving in the Committee of Revision, proposed that the Pharmacopœia be brought into accord with the law by adopting the 9 p.c. standard. This proposition was discussed and defeated, and a standard of 7 p.c. was adopted, for a nation into which opium of less than 9 p.c. could not lawfully come, and for ten years had been prohibited. At this point Dr. Davenport's position would have been that the Treasury Department should have changed the law to accord with the Pharmacopœia standard, and this might then have been done, because, as a Treasury Regulation under the law, it could have been changed without recourse to the Congress. But the conflict thus deliberately brought by the Pharmacopœia between its authority and the law was only an apparent,—and not a real conflict, since the law excluded the importation of drugs that were *inferior* in strength and purity to the standard established by the Pharmacopœia, and 9 p.c. was not inferior to the 7 p.c. standard ; and the object of the law was to increase and not to diminish standards of strength and purity.

At the revision of the Pharmacopœia for 1870,—the 9 p.c. law having then been in operation twenty or more years,—the officinal standard was changed so that opium dried at 212° F. was required to yield at least 10 p.c. of morphine by the officinal process. This standard would be equivalent to about 8 p.c. in the moist condition. Up to, and including this revision the old Staples process of assay was the officinal one, and this gave a fairly accurate account of the proportion of morphine present. Indeed it was the basis of the writer's modification of Prof. Fluckiger's process, having been modified and used by the writer for many years. Thus again in 1870 the Committee of Revision refused to conform to the law and the practice of the General Government, and continued the authority of the Pharmacopœia against the law, but this authority was not harmful while the law excluded opium of less than 9 p.c., since very few persons would reduce the strength of opium as imported, to the officinal standard.

At the revision of 1880,—the law having then been in operation thirty or more years,—the Committee of Revision no longer disregarded it, but intended to come fully up to it by adopting 9 p.c. as the officinal standard, and the intention was also to adopt a more accurate process of assay than the old Staples method. The writer, among others, was invited to contribute to this object of getting a better process, and very cheerfully did much work for the Committee, which resulted in his offering his modification of Prof. Fluckiger's process. This was, however, rejected by the Committee in favor of the present officinal process, doubtless because they considered the latter as better and easier, and therefore better adapted to pharmacopœial use. In practice, however, it has not proved to be sufficiently accurate, its results being variable, but generally, if not always too low; and it is this defective process of assay which now confuses and discredits the pharmacopœial authority.

By an Act of Congress of March 3, 1883, it is declared that "The importation of opium containing less than 9 p.c. of morphine is hereby prohibited." So that since that Act went into force the standard has not been a Treasury Regulation based on the law of 1848,—but has been itself a law of Congress, and as such it cannot be traversed by State laws, nor by the Pharmacopœia. Opium must *contain* 9 p.c. of morphine, and the Treasury Department must ascertain that it contains at least that proportion before admitting it into the country. The question next arises, how shall the Department ascertain this percentage? Examiners are appointed who go over the known processes of assay and select two or more for practical application,—one of these being the officinal process. Two or more Examiners, working month after month upon hundreds of assays,—upon examining results, find that the Pharmacopœia process does not give account of all the morphine which opium contains, and they are therefore bound by the law to prefer any other process which within their knowledge and experience does give all the morphine.

The Treasury Department is bound by the law of 1848 to admit no opium that is "inferior in strength and purity to the standard established by the United States Pharmacopœia;" and is bound by the law of 1883 to admit no opium which contains less than 9 p.c. of morphine. It has obeyed both laws ever since their enactment, and must continue to obey them so long as they are unrepealed, and when the State Examiners ask the Department to ascertain the percentage of opium by the Pharmacopœia process of assay, or by any other that does not give an account of the morphine contained, they ask for an unlawful act, and therefore one that the Department has no power to grant.

The Secretary of the Treasury, in common with importers, cares not at all whose process is used, or what any special process *yields*, but is simply bound by law to see that his experts use the best means known for ascertaining the proportion of morphine which opium *contains*.

If the Pharmacopœia assay could be adopted by the Department it is probable that 60 p.c. of the opium now admitted would be rejected, and yet all but about 10 of the 60 p.c. would contain 9 p.c. or more of morphine. The effect of this upon the importations of opium is easily understood. Importers who have their opium rejected generally appeal from the decision of the Examiners, and the result of such appeals to legally selected experts is final. If the rejections were based upon the officinal process, they would very rarely be sustained by the experts, and thus much trouble, delay and expense would be necessarily incurred, and the Department which should cause this would earn much obloquy.

Opium is a very important medicine in almost universal use in various forms, and is liable to much adulteration. It is therefore among the most prominent substances to be looked after by State Boards of Health, and if their examiners should enter prosecutions based upon the officinal process, which is really their law, the Courts would fall back upon United States law as construed by experts, and then the State laws would often be weakened by defeat where their strength is most needed. The authority of the Pharmacopœia must be right, and be capable of being shown to be right, in order to be sustained by law, and in order to command proper respect.

Mr. C. M. Stillwell has added a practical detail to the writer's method of managing samples of moist opium which tends to greater accuracy and is often a very great convenience. The samples from different lumps which are to be worked into a homogeneous mass are often so soft and sticky as to adhere to the fingers, obstruct the working and involve loss of moisture by the time required. Mr. Stillwell's method, which the writer has often adopted with entire success, is simply to use a little powdered starch upon the fingers and other surfaces upon which the mass is to be worked up. If but little starch is required its weight does not more than counterbalance the moisture lost in the working. But if the mass be very soft, and much starch be required, it is better to weigh off a gram. of it, work it all in, and take account of it in weighing off the portions for the assay.

It is believed that the working up of the mass of samples is not always effectively done, and that this is not infrequently the cause of a variation between two or more assays from the same mass. The shell, or surface of the lumps of opium, is often very dry and hard, the dryness of the lumps diminishing to the centre of each one.

Some lumps in almost every case of opium are quite hard, and to get these hard portions equally distributed through a mass is by no means easy, while if they be not well distributed assays will vary, from this cause, to the extent of one to three-tenths of a per cent.

When a mass has been very thoroughly worked by repeatedly rolling it into a long cylinder and doubling the ends into the centre, and again rolling out, lumps are still to be found in it on close examination, and therefore parts of the mass are almost certainly different, while in the long working much moisture will be lost. Therefore, in cases where it is important to have a closer assay than from one to three-tenths per cent. variation, as in appeals from Custom House decisions, it is best to weigh the total unmixed samples in the tin box as collected and carried, and then dry them until they can be rubbed to a uniform powder, weighing off the portions for assay from this powder.

In all the more recent processes of assay for opium the resulting crystals of hydrate of morphine are directed to be dried at 100°C. with the conspicuous exception of the U. S. Pharmacopœia, which directs that the crystals be dried at 55 to 60°C.

These crystals of morphine contain one molecule or about 6 p. c. of water of crystallization, and the almost universal statements of the authorities are that it does not lose this water below 120°C. and hence the directions to dry them at 100°C. seemed quite safe and proper.

In a paper entitled "Morphine Hydrate, by D. B. Dott, F.L.C., F.R.S.E.," read before the Pharmaceutical Society of Great Britain, at an evening meeting in Edinburgh, on February 15th, 1888, and published in *The Pharm. Journ. and Trans.* of February 25, p. 701, the author shows that the generally accepted authorities are all in error on this point, and that the crystals do lose their water of crystallization even at 75°C., and in time lose the whole of this water at 90°C. or below that.

In the Journal above cited for March 24, 1888, p. 801, there is a "Note on Morphine, by Dr. O. Heese," confirming and establishing the results of Mr. Dott, having previously published, as the result of numerous determinations, that the crystals lose all their water between 90 and 100°C.

From this it will be at once seen that in the writer's process of assay and in all those who followed him, there has been a hitherto unsuspected source of error in the drying of the crystals which must have led to discrepancy in results, because varying mixtures of anhydrous and hydrated morphine have been constantly weighed, compared and stated as hydrated morphine.

In shaking out the crystals, common to almost all the modern processes of assay, the crystals vary very much in size, even from the same opium and management, and as they vary in size they will vary in the proportion of water lost in a given time at 100°C. Therefore the same opium with the same management will vary, from this cause, in the results of assays, and will vary in proportion to time and temperature, so as to affect the results to the extent of .1 to .9 p.c.

Since reading the important papers above referred to the writer has examined closely his customary methods of drying, and has caused some practical trials to be made. The crystals from an assay, air dried, were put into a cold desiccator over sulphuric acid for 48 hours and then weighed. In 48 hours more in the desiccator the 1.7 grammes of crystals had lost .002 gramme. Then in 24 hours more the weight was unchanged. Next, in a steam-heated drying closet at 80° to 82° C. the loss in 4 hours was .42 p.c. In 3½ hours the additional loss was 1.21 p.c. In 2 hours more the additional loss was 1.03 p.c., and then weighed about every 3½ hours the loss diminished until after 22½ hours heating at 80° to 82° C. the total loss was 4.77 p.c. when it ceased to lose at that temperature. Then heated to 90° C. it lost in 2½ hours .546 p.c. additional. In 3 hours more 1.192 p.c. In 2¾ hours more .052 p.c., and then in 11 hours lost no more. Loss at 90° C. 1.790 p.c. Total loss (at 80 to 82° C. 4.77 p.c.+1.790=) 6.56 p.c., which agrees almost exactly with the results of Mr. Dott.

Then in three carefully made assays by different methods, the crude hydrate of morphine crystals were dried at 50° C.,—not until they actually ceased to lose weight, but to the usual extent of 2 or 3 hours,—and were then weighed. Dried at 100° C. and weighed every 4 hours for 16 hours, until they ceased to lose, the loss was for each 4 hours as follows :

Crystals from Stillwell process,	7.02 p.c.	.07 p.c.	0 p.c.	0 p.c.	Total, 7.09 p.c
" " E. R. S. "	6.70 "	.20 "	.087 "	0 "	" 6.98 "
" " U. S. P. "	6.34 "	.47 "	.15 "	0 "	" 6.06 "

By the Stillwell process the crystals being finally washed with morphiated spirit and ether, seem to lose their water of hydration more quickly.

These losses somewhat exceed the first trial, and this, probably, because the drying at 50° C. was not complete.

From these considerations it is plain that the statements of results of opium assays up to this time have all been slightly erroneous from an hitherto unobserved source of error, and that this error has varied with the time and temperature of drying between the limits of about .1 to .9 p.c., and that hereafter this source of error should be avoided.

It may be avoided in two ways,—either by drying the hydrate of morphine at not over 50° C. for 6 to 8 hours;—or by drying at 100° C. for 4 to 6 hours and adding about 7 p.c. to the resulting weight, for the water of hydration lost, by drying at the higher temperature. In either case the drying must be continued until it ceases to lose weight.

As it has always been the usage or intention to state the results in the terms of crystallized morphine, and as crystallized morphine contains at least one molecule of water of crystallization (1½ molecules according to Mr. Dott), it would be very confusing and inconvenient now to change and state them as anhydrous morphine, beside, it would be inaccurate so to do.

The writer proposes now to follow up this subject of drying in his ordinary practice, and ascertain by experience which is the best and most accurate way, with the confident expectation of closer and more uniform results.

An opium has lately appeared in this market which, from having been sent at first to some Boston houses, is called in this market "Boston Opium." Much good opium as well as poor has always been sent to Boston houses, but because this opium is so peculiar as to require a distinctive name, it has become known as Boston opium, although little or none of it may go to Boston since its character has been found out. Some of that seen by the writer is the handsomest opium he has ever seen, and a physician or pharmacist who should once get it, and afterward get good ordinary opium, would be likely to think he had been cheated on the last. The fracture is smooth and uniform, the color, odor and consistence good, and the lumps are put up in excellent order. Indeed to a person in the practice of seeing good opium the first suspicious thing about this variety is that its appearance is too good, because it at once suggests the idea of being made up for appearance, and it evidently is so made up. Usually it yields just about the legal 9 p.c., which is doubtless the object of the make up. Sometimes it falls a little short through unskillful management at its source, and gets rejected. But sometimes it considerably overruns the 9 p.c., doubtless through the same want of skill in the make up.

It however need never deceive any one who knows of the existence of such a variety of opium in the markets, because its very handsome appearance and unusually good sensible properties serve, so far, to distinguish it at once.

The object of this note is to make this comparatively new opium better known. It is said to make a very handsome powdered opium, and if so, would be likely then to deceive the most expert judges.

CITRATE OF IRON AND STRYCHNINE.

The Pharmacopœia of 1870, yielding to the popular demand for ready-made arbitrary combinations, introduced the citrate of iron and strychnine, and the present revision retained it, adding a very good paragraph of description and tests.

The preparation is a simple mixture of citrate of iron and ammonium with citrate of strychnine,—or of an iron salt with a strychnine salt, without any known advantage, but with the rational disadvantage of a fixed relation between two agents which are rarely needed in the same proportion or for the same length of time in any two cases.

Its usage seems to depend upon its convenience to those physicians who prefer to have the proportions of their agents fixed for them beforehand. The original intention of the mixture was, doubtless, that it should be given in the solid condition, in powder, pill or capsule, but of late it has become common to give it in solution, and it is the object of this note to state that it is not permanent in solution.

When made in strict accordance with the U.S.P. process a whitish deposit will begin to settle out within two or three hours' and will continue to increase at the bottom of the solution during many days. A slight increase in the proportion of ammonia or of citrate of ammonia will retard the decomposition for a short time, and will redissolve the precipitate when formed, and in this way it may be made to stand about a day or two longer for each 2 p.c of citrate of ammonia added to replace as much citrate of iron and ammonia, but no proportion tried has rendered the solutions permanent for a longer time than three or four days when the proportion of strychnine is kept at 1 p.c. The precipitate in every case was about 50 p.c. strychnine, and any patient who should get the last doses from a vial that had not been well shaken at every dose, would be surely poisoned by the strychnine;—not fatally of course, because if the precipitate was all strychnine and if all the strychnine was deposited, it would require 50 to 100 grains to yield a fatal dose. Yet the effects might be alarming and troublesome.

BAD PRESCRIBING AND STILL WORSE DISPENSING.

The writer was recently summoned as a witness in a New York Court, and heard the following case:

A physician gave a patient for colic one-third of a grain of sulphate of morphine by hypodermic solution in the walls of the abdomen, and gave him a prescription for "Mistura Squibb 2 ℥" to be taken as directed. The verbal directions given with this were that if, on reaching home, the man's pain was better, he should take none. If about the same, take a teaspoonful; if worse, take two teaspoonfuls. In a few minutes after the man left it, the pharmacist came to the physician's office to ask what "Mistura Squibb" was, or what was meant by it. The physician gave him the formula for the common compound tincture of opium or diarrhœa mixture. He knew what that was, and went off to dispense it. A short time after he came to the physician again, and said he had made a great mistake by having dispensed the compound solution of opium, a preparation six times stronger than that intended, and containing a proportion of opium equivalent to about 7½ grains of sulphate of morphine to the fluidounce.

They at once sent for the patient to come to the pharmacist's store, when they found he had taken two teaspoonfuls of the compound solution of opium, about equivalent to two grains of sulphate of morphine, after having had one-third of a grain by hypodermic injection. The gravity of the case was at once realized, and very vigorous, proper measures were adopted to counteract the opium; and after two physicians walking and dragging the patient through the streets all night with occasional bowls of strong coffee, —keeping near to a large hospital where a battery was in readiness in case the respiration should entirely fail,—signs of improvement began. Then in a few hours more the danger was past.

It seems altogether inexcusable for any physician to write such a line as that above quoted and issue it as a prescription, because it really indicates nothing, and means nothing that any pharmacist is bound to know, or can in any way be responsible for not knowing. If physicians by thoughtless habits abbreviate and curtail their names so that they signify nothing with definiteness or safety,—and will use names of persons instead of things, or proper names as indefinite adjectives,—they not only discredit themselves, but also their profession, and when they get into the Courts they can expect no mercy.

The pharmacist in this case did exactly what was right, and took the only proper course open to him, when he went to the physician with his nondescript prescription, for an explanation, and the physician then did the best he could do by giving him the formula for it. But, after this, the pharmacist went back and committed the almost criminal blunder of dispensing a solution instead of a tincture, the one six times stronger than the other,—with the formula for the weaker one in his hand, and the label of the stronger one on his bottle,—with a nearly fatal result.

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VOL. III. No. 4.

AN
EPHEMERIS
OF
MATERIA MEDICA, PHARMACY,
THERAPEUTICS
AND
COLLATERAL INFORMATION.

JULY, 1889.

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1889

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DIPHTHERIA.

The Kings County Medical Association, over which the writer has had the honor of presiding through the last three terms, concluded, at the April meeting, a discussion of diphtheria, which occupied with interest and profit, six consecutive monthly meetings. The importance of this discussion will be recognized from the fact that during the time occupied by it, no less than 594 deaths occurred from diphtheria in an estimated population of about 800,000; and from the circumstance that many of the best and busiest physicians of this population took part in the discussion. The monthly accounts of this discussion will be found in Gaillard's Medical Journal from November, 1888, to June, 1889, inclusive. All that is aimed at here is to give a brief abstract of the materia medica element of the discussion, so far as the principal agents used are concerned, and these agents will be taken up in the order of the frequency with which they are used in this locality. This, however, may not be the order of their real importance in treatment, because some have a popularity from long established use, which may be yielding to more recent agents. In almost all cases more than one of the agents were used.

ALCOHOL was almost universally used, and generally as brandy or whisky, but with two very distinct objects in view. The greater number of physicians used it in moderate quantities as a stimulant and a food to support the failing powers of their patients, and in the more exhausting stages of the disease, and always as an adjunct to other active treatment. But there were many who used it in large quantities from the very onset of the disease, as a special, powerful antidote to the malignant poison of the disease very much in the way that it is used in snake-bite. This treatment was pursued and strongly advocated by the late Dr. E. N. Chapman of this city up to the time of his death. Long before his death, however, he published a monogram on "The Antagonism of Alcohol and Diphtheria," Brooklyn, 1878, at which time he had treated 125 cases with but one death. Many have followed this use of alcohol, as the principal element in treatment, with encouraging success, but not generally with the success of Dr. Chapman. One busy and successful physician, who had long used this treatment, during an epidemic in his practice, awoke one night at 3 A.M. with easily recognized symptoms of diphtheria, including a membrane in the pharynx. He at once took half a bottle of brandy,—probably about 12 fluidounces. This under ordinary circumstances would represent about 5.4 fluidounces of absolute alcohol, or about the fatal dose. By 8 o'clock,—or in 5 hours,—he had finished the bottle of say over 10 fluidounces of absolute alcohol. After such a use of alcohol he was "at work again in a week," and he believes that it saved his life. And yet when in health half an ounce of brandy makes him feel "heady." Most of those who used alcohol in this way testified to the absence of any signs of intoxication when the disease was at all pronounced in degree; and any signs of intoxication, or odor of alcohol on the breath were regarded as the limit of dosage. From 6 to 12 fluidounces of brandy in the 24 hours were not infrequently used on children from 6 months to 3 years old, though in the larger part of a general experience much smaller quantities were required :—but always alcohol from the first in liberal and frequent doses.

TINCTURE OF THE CHLORIDE OF IRON was perhaps the agent next most commonly used as a principal element in treatment, by the greatest number of practitioners, and this was always used freely as both a local and systemic agent. Though rarely used alone, there was much testimony in its favor, and none against it. It was simply losing ground to agents that were gaining in popularity.

CORROSIVE SUBLIMATE, or mercuric chloride, was very largely used as a local application by spray or gargle,—about 1 to 500 for spraying, and 1 to 4,000 for gargling. A large number of physicians used this agent locally, and a smaller number used it systemically. In no case had there been toxic effects, and in one case, only, there was mild salivation, and the experience from its use was generally favorable. When used internally, the doses were generally small and frequently repeated, and the administration was carried to the production of the characteristic diarrhœa with green stools. Attention was called to a recent paper on "Mercuric Bi-Chloride in Diphtheria," by Dr. John S. Coleman, of Augusta, Ga., published in the Journal of The Am. Med. Asso. for February 23d, 1889, page 254. Dr. Coleman claims for mercuric chloride what has been, by others, claimed for alcohol,—that diphtheria establishes a tolerance of the agent, and certainly his experience tends to sustain such a claim. Among other cases he relates one of a child 16 months old who took corrosive sublimate in doses of one-eighth of a grain hourly for 72 consecutive hours,—9 grains in three days,—with the result of complete recovery after expelling a large tube of laryngial membrane. This was his largest dosage, and his worst case, but other children took very large quantities with similar results. A child of three years took six eighths of a grain in 6 hours, and a total of 10.5 grains in 9 days. Any such quantities in healthy children would probably prove fatal.

Dr. Coleman does not always use such doses, but begins with one thirty-second of a grain and increases until the disease is counteracted or is in abeyance. It was stated by a member who knew him, that Dr. Coleman was not an enthusiast, but an old long-established physician not likely to be carried away by having a theory to support.

Peroxide of Hydrogen, or hydrogen dioxide, was presented during the discussion, as having been used both locally and internally in the treatment of diphtheria, as being one of the most active and energetic antiseptics known, and some account of it is given in this pamphlet at page 1146. It was subsequently used by several of the members, and the reports of its use then and since have been very favorable. Without being new at all, it is being treated as a novelty, and many very extravagant statements are being published by the makers of it, so that it is feared that this may prejudice the use of what should, on principle, be a very valuable agent, not only in diphtheria, but in many other septic conditions.

As an ultimate result of the whole discussion it may be fairly stated that with the use of these agents, judiciously applied, the fatal cases of diphtheria, in the hands of those who discussed it here, were very far below its general mortality, and as this came to be apparent from the discussion it was questioned whether this was the result of treatment, or whether it might not be the result of a milder form of the disease in the classes of the community among which these physicians practiced. There was, however, no doubt left in the minds of any as to the value of treatment in contrast with expectant nursing of the sick,—and in this connection the writer offers no apology for quoting the weighty words of one who has observed diphtheria as closely, seen as much of it, and written upon it as intelligently as any living authority.

Dr. A. Jacobi, of New York, in addressing the British Medical Association,—see *The British Medical Journal* for September 22, 1888, page 653,—says:

"In urging upon you these remedial measures in the dangers of diphtheria, I beg of you not to take me for a meddler and interferer. Like yourself, I see many a case of sickness, and treat many without medicines. But there must be a reason for both non-medication and medication; and there must be medication when there is an indication for it. When there is, there is also an indication for a sufficient dose. I believe in Nature, and in spontaneous cures, but I know also that Nature destroys with the same equanimity and indifference with which it allows the getting well. I believe in the action of medicines, and the responsibility of the physician; I know that when a political Nihilist commits a single murder the newspapers of the world talk loudly of it. When a therapeutical Nihilist commits a hundred homicides, a quiet certificate and the silent sod cover the sins of omission."

I.

EVOLUTION OF COMMUNICABLE DISEASE AND ITS MANAGEMENT.*

By E. R. Squibb, M. D., of Brooklyn, N. Y.

The thorough discussion of the character and management of diphtheria by this Association has demonstrated the fitness of this disease to serve as a type and illustration upon which to base some

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*Read before The Kings County Medical Association, February 5th, 1889, during the discussion on diphtheria, and published in Gaillard's *Medical Journal* of March, 1889, p. 257.

generalizations and some reasoning which may be both in time and in place here.

Diphtheria appears to have been slowly evolved during the past three centuries by a gradual, molecular accumulation or grouping of its elements, just as chemical elements group themselves into new molecular forms under new conditions. Constituent characteristics of the now specific disease came together from time to time, first in sporadic cases, then endemically, and finally in epidemics; but only in the early part of the present century acquiring sufficient identity to be recognized as a specific disease under its present name.*

Then, as named by Bretonneau from one of its most constant products, it was still short of its present character. Its epidemics were numerous enough, but with no distinct evidence of communicability. Even when it invaded this country as late as 1857, or thereabout, it rarely appeared to be contagious. Now it is recognized by all as a most definite, specific, contagious disease. In short, diphtheria has been evolved from scattered elements into a concrete disease within a period of time that is traceable in the history of medicine. A period in its history is easily reached when there is no mention made of its communicability. Then it became of doubtful communicability. Now it is undoubtedly contagious by means of its products. How did this communicability arise? It is the most important characteristic of the disease, because without communicability it would be comparatively harmless.

Here then is a specific disease which has been acquired by the human race during the few centuries embraced by intelligent medical history; and its most important characteristic; namely, its contagion, has been acquired within a single century, and has within that time grown to its present degree. Other diseases seem to be acquiring communicability in the same progressive way,—pneumonia and phthisis, for example,—and another century may bring these to a degree of communicability equal to that of diphtheria now, and may advance diphtheria to the degree of small-pox.

If health be the normal condition of the race, then disease is abnormal; and if such abnormality be acquired, it follows, that under other and better conditions, diphtheria would not have been

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*As late as 1862, Dr. William Aikin in *The Science and Practice of Medicine*, London, 1863, vol. I., p. 565, seems to have confused other affections with diphtheria—since he says: Towards the middle of the last century it was prevalent in America, and particularly at New York and Philadelphia. "It terminated the life of the celebrated Washington, and of the Empress Eugene."

acquired as early, or might not have been acquired at all. Again, under such better conditions the communicability of the disease might have been developed at a later period of its age,—might have progressed more slowly,—or might not have been acquired at all. The agency by which it is communicated or propagated,—the contagium,—could not have existed before the time when it became communicable;—or, the condition capable of being impressed by the contagium,—the susceptibility,—could not have existed. Therefore this contagium and the susceptibility to it must both have had a beginning and a development or growth. But, a contagium without susceptibility to it, is unknowable; while a susceptibility to disease, as the first step in any departure from normal health, is easy to comprehend, and upon this the beginning and growth of a contagium is easily understood.

If the contagium be a living organism, one of two primary conclusions must be accepted. The organism must have had a beginning, and that is a new creation for each contagious disease at the time when it becomes contagious; but spontaneous generation is not now accepted;—or, the living organism must have been evolved from some pre-existing organism by gradual change of pabulum, and through this change of surroundings (environment), must gradually have acquired its new powers of contagion.

But this latter conclusion is only logically tenable on the ground that the diseased condition, or the susceptibility to it, endows the organism with the power to propagate the contagium, and thus it really carries the power behind the organism to its pabulum or environment. Then, as the pabulum, which changes and evolves the organism, must precede the changed condition and power of the organism, it is only rational to infer that the pabulum may be the virus of contagion, and the organism may be the consequence and not the cause of contagion.

Or, the pabulum,—itself unable to propagate contagion,—may so nourish or cultivate the organism as to give to its products the power of contagion.

Again, it is not irrational to suppose that neither the pabulum nor the organism, separately or together, have the power of contagion; and yet the products of the organism, or the combination of such products with the pabulum, may be the contagium.

In any logical, inductive consideration of the acquired power to propagate disease, it must be conceded that the susceptibility, or condition of pabulum, antedates or precedes all other elements in the chain of causation, be these elements few or many, and that the virus of contagion is not simple but complex.

Whatever may be the nature of the virus of contagion, or however potent or perfect or virulent it may be, its action and effects are very inconstant. No case of contagious disease ever affects all who come within the influence of the contagion, as would be required by a perfect contagium. Even in severe epidemics a very small proportion of those subjected to it are affected by it at all in any of its varying degrees. This re-introduces the quality of susceptibility in its relation to the spread of contagious disease.

All the way down the centuries through which disease is evolved, it is constantly opposed by the persistence of the type of normal health,—the natural tendency to be well, and to return to health when sick. But throughout these centuries a susceptibility to disease has been gradually acquired against the tendency of normal health to persist, and this susceptibility is more important than the contagion, because it generates the pabulum upon which the elements of the virus of contagion originate, and upon which they develop into full power.

The superior importance of this susceptibility is again seen in the self-evident fact that by controlling it at any stage or degree the whole train of disease, including communicability, is controlled.

The management by which increasing knowledge and skill has sought to control disease, has, through a process of evolution, gone on parallel with disease, and has thus brought the race to its present condition of civilization. This management has always been of two kinds. First in order of origin and practice was the control of disease when it occurred; and second, the control of the causes of disease so as to prevent its occurrence. Only in one branch of this last subdivision of management has the progress seemed to be slow, and to have fallen behind the rate of progress of disease. Neither the sickness rate nor the mortality of the earlier ages of life has been reduced in the same proportion as in adult life, and although the lower rate in adults may depend largely on the fittest having survived, yet this does not account for the entire difference. This very important remainder will doubtless be found in the defective management of the health of early life through which the susceptibility to contagious diseases is kept at a high point.

Contagion, however mild or virulent, affects a very small proportion of those exposed to it, and affects the few in various degrees of severity, quite irrespective of the mildness or virulence or the quantity of the contagion. These conditions are expressed by the varying degrees of susceptibility in those exposed to contagion; and this varying susceptibility is but an expression of varying powers of vitality, or of persistence of the type of normal health.

Children are born with an immense power to live and thrive. That power which in 280 days increases the weight of the fœtus more than 280 times, continues after birth. The fœtal mortality rate is very small, and although the mortality rate of the newly born is greater, it is still very small during the first few weeks of independent life, and the susceptibility to disease is very low—not much higher than during fœtal life. All that appears to be needed now is to utilize, economize and continue this momentum of normal vital power, and its consequent low susceptibility, as the condition upon which a normal childhood and adult age are to be expected.

But at birth it becomes optional with the mother whether or not she will continue to nourish her offspring by supplying the natural food of the second stage of life. Occasionally through hereditary descent from mothers who have not nursed their children, or through individual defects, mothers cannot nurse their children. Occasionally they think they cannot, or are badly advised, and do not try. Again, they try, and through want of persistence think they fail; and so on, until now, under one pretext or another, a large proportion of mothers do not nurse their children; while another class, from easily preventable causes, nurse them badly or insufficiently, and thus the mammary glands seem to be slowly degenerating to the rudimentary condition.

Under these circumstances—milk being so plainly the food for all mammalian young,—the milk of healthy animals that have lost no part of either their organs, functions, or instincts of maternity, becomes the natural and rational substitute,—and, fortunately, this substitute is always within easy reach of those classes of the race that most need it. But here mercantile interests, and the ingenuity, plausibility and credulity begotten of such interests, come into play, and artificial substitutes for the natural substitute are offered and urged in increasing numbers.

These artificial infant foods, as often as they have been examined with the requisite knowledge, care and skill, are found to consist mainly of flour and sugar, and they are all abnormal and unnatural as applicable to the young, whose natural food is milk.

That no mammalian mother ever produces such mixtures, or anything at all analagous to them, should be a sufficient answer to all their claims and to the certificates of the prominent medical men who counsel their use. Yet their use has become so general that it is quite time to consider their possible or probable relation to the susceptibility of childhood to disease in general, and especially to contagious diseases, like diphtheria.

The influence of unnatural and defective food upon the young is too well known to need discussion. In a large proportion of cases the primary effect seems to be to compel the using up of the reserve stores of vital force, without producing immediate sickness, and generally without appearing to interfere much with the early development, so that there is little or no evidence that the tendency of health to persist through these vital reserves, is being used up until infancy is past, and the defective power of resisting disease is shown in a commencing susceptibility.

That the sickness rate is low in early infancy when artificial foods are used, and high after these have been replaced by a varied diet, is not a sound argument in favor of such foods, because by having caused the reserve forces to be used up, and by having vitiated the natural appetite for more wholesome food, the artificial foods may have left little power to resist disease, and this without much apparent deviation from health. Thus a high rate of susceptibility may be cultivated in individuals and in communities, unsuspected because unseen, until shown by attacks of sporadic or epidemic disease, and by the more or less feeble resistance to such attacks.

Whatever weight may be accorded to the above reasoning, certain conclusions having an important bearing upon the management of communicable disease, can hardly be avoided.

First.—Susceptibility to disease must precede diseased action; and the causes of disease, whether communicable or not, must be evolved from this susceptibility.

Second.—This susceptibility is acquired upon a normal basis of health, which basis has a normal tendency to persist or to resist, and therefore the susceptibility is preventable.

Third.—This susceptibility varies in degree from insusceptibility up to the highest rate; and the degree of activity or virulence of contagious virus must coincide with the degree of susceptibility in the production of disease, either factor being impotent without the other.

Fourth.—In controlling susceptibility, the virus of contagion and other causes of disease are necessarily controlled.

Fifth.—Susceptibility is acquired gradually and imperceptibly through a process of evolution, and its control or management must be through a similar process.

The practical deductions to be drawn from these conclusions constitute the object of this note.

Without any relaxation of effort for the treatment of communicable disease as it occurs, for the destruction of the virus of contagion, and for the protection of susceptible individuals, persistent effort should be made in another direction not commonly considered ; namely, to lower the rate of susceptibility. In every community physicians see examples of successive generations of well-ordered lives in the rearing of offspring in a rational, nearly normal way, and see that in a broad average such always show themselves fittest to survive. All such examples, and all that approach them, should be encouraged, supported and multiplied.

One of the increasing defects of late generations seems to be want of proper parental discipline and training of the young. Education, without power behind it to enforce its teaching, is not sufficient to restrain from injurious inclinations and appetites.

Children are perhaps very generally taught that self-denial, and not self-indulgence, must be the order of well-lived, healthy lives. Yet upon this teaching the cultivation of perverted appetites and the indulgence of them, is the common practice ; and as candies and cakes take the place of more simple and wholesome natural food. artificial digestives are required, and conditions are gradually established upon which disease is more frequently and more easily acquired, and upon which disease itself is gradually developed and intensified into a more frequent and more easy communicability.

The doctrine that disease is penal, and that as a penalty it is always earned and always sure, is not only true upon the grand scale of the past ages, but is a good working hypothesis for the present time. The practical utility of the doctrine is however much weakened by the circumstance that the offences of one generation are entirely or mainly punished in succeeding generations. In this remoteness of causes from their consequences, their connection fails to be realized at its actual value, yet all vital processes are based on absolute justice and truth, and, as is well said by Emerson, the universal law of transgression is retribution.

Hence it would appear that the control of disease must be by a process of evolution incited and fostered mainly in the management of the young, that is, of the commencing generations, where control is at once easiest and most effective.

It is said of Dr. Oliver Wendell Holmes that when asked how early the training and discipline of children should begin, he replied, in substance, very early indeed; with their great grandparents; an answer that is as full of wisdom as of wit.

II.

DISINFECTION BY BURNING SULPHUR.*

By E. R. Squibb, M. D.

Under the head of Prevention Dr. Segur asks what are the important measures of prevention: and among these may certainly be included the disinfection of infected apartments.

Perhaps the most common measure for the disinfection of apartments which have been infected by diphtheria and other contagious diseases, is the burning of sulphur. This mode of disinfection has been in active use for more than a hundred years and many epidemics of contagion are supposed to have been controlled by it. Of late years, however, its efficacy and utility have been called in question by several prominent authorities on the ground that it does not prevent the development of the spores of several microbes supposed to be pathogenic of important contagious diseases.

If it be admitted that the burning sulphur was properly applied, and that the propagation of the spores is positive proof of persistence of contagion, then the question must be considered as settled and the practice should be abandoned. But as the first of these propositions, at least, cannot be safely admitted in the attempts at disinfection as commonly practiced; and as the method is continued by Boards of Health and hospital authorities as well as in private houses, notwithstanding the evidence against it, it may be useful to re-examine the conditions to be met.

In a given locality there are particles of contagious matter so small as to float in the air, and these settle upon, or become entangled in all surfaces to which the currents of air carrying them have access. . For perfect disinfection the contagious element or virus of all such particles must be so changed as to be no longer contagious. This change must be effected either by physical or by chemical action, or by both acting together.

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* Read before The Kings County Medical Association, February 5th, 1889, during the discussion on diphtheria, and published in Gaillard's *Medical Journal* of March, 1889, p. 268.

It seems to be absolutely proven that the one element necessary to the activity of all virus is moisture. Desiccated virus is inactive and impassive; and when desiccation is complete or perfect, as by a sufficient degree of heating for a sufficient length of time, the change is such that the re-supplying of moisture does not reproduce the contagion.

But moisture is an element of varying degree. Too much by dilution may weaken active virus to absolute inactivity, as too little may weaken it to practical destruction.

Contagious matter or virus which is only sufficiently dry to be thus rendered inactive and impassive, becomes active by contact with moist surfaces, and thus moisture becomes the essential element in its contagiousness by supplying the conditions under which its molecules can resume the function of propagation or generation. This same element moisture, which is necessary to enable them to propagate contagion, is equally necessary for any reaction with agents which have the power to so change their molecular structure as to destroy their capacity for contagion.

Hence all disinfectants require the presence of moisture, and require it in a degree sufficient to enable all the molecules of contagious matter to commingle and react with the molecules of the disinfectant. If the moisture be sufficient in amount it matters little whether it be held by the virus or by the disinfectant, but the reaction will be much more sure and more prompt if each of the reacting substances be fully saturated with moisture. If either agent be dry or nearly dry, the reaction will be proportionately slow and imperfect.

The condition of the contagious material of an infected apartment, although not absolutely dry, has only the moisture of the common atmosphere, and if there was any such thing in the living animal as a dry surface there could be no infection from such air-dry contagious material.

An air dry disinfectant or antiseptic is equally inactive and impassive, and for the same reasons; namely, the absence of the physical and chemical conditions for reaction.

When sulphur is burned in air a dioxide of sulphur is formed. One atom unites with two atoms of the oxygen of the air to form an anhydrous, or perfectly dry gas which occupies practically the same space as did the oxygen combined. This sulphur dioxide is therefore a heavy gas, and as it cools after being formed by the combustion, it falls, so that any enclosure in which it is formed will fill up from the bottom as it would with water, and but for the laws of diffusion of gases, an enclosure might have the pure gas at the bottom and none at the top. The laws of diffusion, and the currents of air and gas caused by the heat of combustion, do however carry the gas to all parts of an enclosure and yet the gas is in greatest proportion near the floor, and any leakage there, as under the doors for example, will waste much more gas than the same openings higher up.

The sulphur dioxide formed is a perfectly anhydrous or dry gas and is therefore called sulphurous anhydride. It is not an acid, but is an indifferent, inactive, impassive gas, showing but a feeble tendency to combine with anything, or to exert any power. It has a moderate affinity for moisture, and when one molecule of the gas combines with one molecule of water sulphurous acid is formed ; when combined with more than one molecule of water a liquid sulphurous acid is formed of a strength proportionate to the amount of water. This solution of sulphurous acid is commonly called simply sulphurous acid, and as found in the markets it commonly contains from 3 to 6.5 p.c. of true sulphurous acid, or the compound molecule made up of one atom of sulphur, two atoms of oxygen and one molecule of water. This sulpur dioxide, or sulphurous anhydride plus water, or sulphurous acid, unlike the inactive dioxide, is a very active and very potent substance, and its prominent characteristic is its affinity or appetite for oxygen, by which it is converted into sulphuric acid. This affinity for oxygen by which it takes that element from all its looser combinations, makes it a powerful deoxidizing agent. And, by taking oxygen away from its looser combinations in the infective matters, it breaks up their complex molecules, destroys their power of contagion, and thus becomes disinfectant. Again, instead of taking away oxygen from compound molecules it may unite with this oxygen and thus form sulphuric acid as a new component of the compound molecule, changing this so as necessarily to destroy it and therefore be disinfectant.

All this detail is to show that sulphur dioxide, resulting from burning sulphur in the air, is not a disinfectant, but requires the presence of moisture either with the sulphur dioxide, or with the infected matter, or with both. And, farther, that in proportion to the amount of moisture up to what would be a very large dilution, the more there is present the more perfect are the conditions for thorough disinfection ; and the less moisture there is present the more imperfect the disinfection.

Now, if the practice of Boards of Health and other authorities be examined, it seems to be very defective indeed, unless they use an abundance of watery vapor without thinking it worth while to mention it in their directions and practice.

The common usage seems to be to close up the infected apartments as thoroughly as practicable and to burn sulphur in them in the proportion of four pounds of sulphur to each 1,000 cubic feet of space.

There are no directions to stop up the lower chinks more carefully than the upper ones, while the lower half of a door will waste twice as much gas as a window. The sulphur is usually put in an iron pot or pan, and this is set in a larger vessel of water or upon a vessel of wet ashes or sand ; and this seems to be done to lessen the risk of fire rather than to supply vapor of water. The sulphur is lighted by means of alcohol poured upon it and lighted, and the apartment is then closed and watched until the sulphur is burned out. The dioxide formed finds a little moisture in the normal atmosphere of the room, and thus a small proportion of it gets converted into the active sulphurous acid. Then the heat of the burning sulphur vaporizes a portion of the water in the vessel in which it is placed. Under favorable conditions the amount of water thus vaporized may equal or slightly exceed the weight of the sulphur burned. But under general conditions it will be much less. These two sources being the only ones from which moisture is supplied, and the amount supplied being very much too small, it is only reasonable that the disinfection should be proportionately incomplete, and under such conditions any condemnation of sulphurous acid as a disinfectant is unsound and irrational.

The conditions for a much better application of this agent are very easily supplied. To fumigate with the active sulphurous acid, instead of the inactive dioxide of sulphur, it is only necessary to evaporate water to the extent of three or four times the weight of the sulphur burned, or to wet the surfaces to be disinfected, or both, so that plenty of moisture may be present during the burning of the sulphur. A shallow pan of water upon a kerosene stove well started in advance of lighting the sulphur, and the floor, ceiling and walls well sprinkled with water by means of an ordinary dust-brush, is perhaps as good a practice as any.

There is abundant evidence on record that sulphurous acid in small amount is destructive to all the lower orders of animal and vegetable life, to all fermentations both vital and chemical; and, all that the more recent elaborate investigations seem to have shown, is, that the spores or germs of certain microscopic organisms were not destroyed by it as applied to them, even in the presence of abundant moisture in some of the trials. Many of the late investigations have been made with very great care and labor and by modern accurate methods. Some of the best results are, however, confusing, if not contradictory, and, therefore, are inconclusive, even in regard to the resistance of spores.

Chiefly from the above-mentioned considerations the writer reaches the conclusion that burning sulphur for disinfection should by no means be abandoned, but should be more thoroughly and more carefully applied.

Not only in diphtheria, but in all infectious diseases some such disinfectant is greatly needed in preventing the spread of disease, and diminishing the risks of susceptible persons, and no other method has yet been proposed that is more effective, more simple or of easier application.

In the less convenient and more costly method of disinfecting by gaseous chlorine the same principles apply, and the same conditions are necessary. Dry chlorine gas is as inactive as sulphur dioxide, and from deficient supply of moisture the one will fail as often as the other.

When chlorine is generated from common salt by means of dioxide of manganese and sulphuric acid, the salt and manganese are commonly mixed into a thin paste with water before the acid is added. Then on adding the acid much heat is developed, and a proportionate amount of water is evaporated and disengaged with the chlorine. But this amount of water is far too small for the full effect of all the chlorine, and unless all the surfaces be well wetted, and steam be supplied, the disinfection will be defective.

If the walls and ceilings of apartments be kalsomined, or be covered with any other preparation of glue or paste, these should be scrubbed off clean with hot water before the disinfection, because disinfection does not destroy the tendency to putrescence in gelatine, glue, paste, etc.

III.

ON THE MEDICINAL USES OF HYDROGEN PEROXIDE.*

By E. R. Squibb, M. D.

Throughout the discussion upon diphtheria very little has been said of the use of the peroxide of hydrogen, or hydrogen dioxide, yet it is perhaps the most powerful of all disinfectants and antiseptics, acting both chemically and mechanically upon all excretions and secretions so as to thoroughly change their character and reactions instantly. The few physicians who have used it in such diseases as diphtheria, scarlatina, small-pox and upon all diseased surfaces, whether of skin or mucous membrane, have uniformly spoken well of it so far as this writer knows, and perhaps the reason why it is not more used is that it is so little known and its nature and action so little understood. Until within the last few years, except in a few manufacturing processes, it was chiefly known as a chemical curiosity, rarely seen because difficult to make. Too long known to be a good subject for a patent, or for any kind of excitement, it was not made in large quantities and most of it went to secret uses. The fact that upon principles well established, it was a most active disinfectant and therapeutic agent, seemed to count for very little. Now, however, it is made in large quantities by several manufacturers, and is quite accessible to those who choose to take a little trouble to get it of good quality.

In order to use it intelligently both the pharmacist and the physician must know something of its nature and properties. The name hydrogen dioxide expresses its composition, and its formula H_2O_2 represents this name. Hydrogen monoxide, H_2O, or water, can under certain conditions be made to combine with a second molecule of oxygen, the result being a water-like liquid, H_2O_2.

This second atom of oxygen is very loosely combined, and the compound molecule is always on a strain to break up into water and oxygen, and when it breaks up, either slowly or rapidly, the oxygen separates in that nascent or most active and potent of its conditions next to the condition known as ozone. It is in the change of this breaking up into water and active oxygen, that the latter element exerts its power, and the simple contact with organic matters, which are themselves of complex nature and in condition to be changed, is sufficient to break up the dioxide and liberate the active oxygen. For example, some albuminoids are instantly changed by contact with hydrogen dioxide, as is shown by rinsing the mouth with a dilute solution, when the albuminoid matters of the secretions are at once coagulated. Then, as all virus is albuminoid, whether propagative or not, it is destroyed, or by coagulation rendered inert, by simple contact with this agent, just as it is by contact with corrosive sublimate. This simple experiment of rinsing the mouth with a dilute solution of hydrogen dioxide and examining the discharged liquid can hardly fail to convince any one of the destructive potency of this active oxygen on some albuminoids, and of its thoroughly cleansing effects upon the mucous surfaces.

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* Read before The Kings County Medical Association, February 5th, 1889, during the discussion on diphtheria, and published in Gaillard's *Medical Journal* for March, 1889, p. 267.

Now, if diphtheria be at first a local disease, and be auto-infectious —that is, if it be propagated to the general organism by a contagious virus located about the tonsils; and if this virus be, as it really is, an albuminoid substance, it may and will be destroyed by this agent upon a sufficient and a sufficiently repeated contact.

The undiluted liquid hydrogen peroxide is from its nature very unstable, and breaks up on very slight disturbance with almost explosive rapidity. Hence it is never made nor used undiluted, but is always dissolved in, or diluted with, water; and what is known in common parlance as "peroxide of hydrogen," and prescribed and dispensed as such, is really a solution of the liquid in water containing a small proportion of hydrochloric acid, the acid being useful, or rather indispensable, in protecting or preserving the solution from rapid change. The strength of the solution is commonly indicated by the volume of active oxygen that a similar volume of solution will yield in use. For example, a solution that will yield its own volume of active oxygen is called a one-volume solution, and from this strength up to a solution yielding fifteen times its own volume, is the practical limitation of the market. The best makers generally send out a fifteen-volume solution and the strength by volumes is given on the label. This solution labelled simply "Peroxide of Hydrogen," is put up in pint bottles which contain about 15 f℥, or 15 avoirdupois ounces, and these are sold at $9 per dozen bottles. It is as colorless and odorless as water—or very nearly odorless. The first taste is simply mildly acidulous. Afterward there is an impression rather than a taste, which resembles nothing and is therefore indescribable. It is not a very strong impression nor a very disagreeable one, as made by a fluidrachm held in the mouth for a minute, nor is the changing after-impression very lasting, and it would be generally less objectionable than most medicines. Changes in this solution are indicated by gas bubbles rising through the liquid or adhering to the sides of the vessel, and by pressure within the bottles. At or below 15°C., or 59°F., this solution does not change materially within any reasonable time. But at 20°C., or 68°F., it does change—often pretty rapidly, by giving off its active oxygen and becoming finally reduced to simple water— and, upon the rapidity of this change at body temperature, depends its prompt and energetic action. Hence it follows, that to be effective it must be kept in a cool place. The stock bottle from which the dilutions are made should be kept in a cool cellar or refrigerator, and the dilutions in use should be kept outside the window in winter or in a bath of ice-water in summer, and when carried from the pharmacist to the patient, the bottle should not be grasped by the warm hand for any very considerable length of time. The bottle may be carried by the neck, or by a string tied around the neck.

The original fifteen-volume solution is never used undiluted. Even as an external application to indolent ulcers or specific sores it is much and variously diluted. Although devoid of danger in application, and hardly irritant at all, it is still useless to apply solutions of a strength greater than needed. A one-volume solution, made with one fluidounce of the fifteen-volume solution in a pint of water, is strong enough for many purposes, but a two fluidounce in the pint, or a two-volume solution for children, and a three fluidounce in the pint, or a three-volume for adults, are perhaps commonly required. In the administration and management of all solutions the contact of all metals must be avoided, because most metals are rapidly oxidized and taken into solution yielding poisonous solutions. All kinds of spray and injection apparatus can now be easily obtained with fittings of hard rubber or glass, and such only should be used.

A child's nostrils, pharynx and mouth may be flooded every two or three hours, or oftener, from a proper spray apparatus, with a two-volume solution, without force and with very little discomfort; and any solution, which finds its way into the larynx or stomach is beneficial rather than harmful, and thus the effect of corrosive sublimate is obtained without its risks or dangers. Adults, and children old enough to gargle the pharynx, and rinse the mouth, will get a better effect in this way, equally without much discomfort, from a three-volume solution, and this applies not only to diphtheria but also to scarlatina and other conditions of mouth and throat which require cleansing and disinfecting. As vaginal injections in cases of uterine cancer, etc., the strength must be increased until the disinfectant effect is obtained. A copious flushing out with a one-volume solution will often be sufficient. When wetted cloths are laid over external sores an over-covering of oiled silk should be used.

As in passing through several hands after leaving those of the maker, a little mismanagement may spoil the solution, some easily applicable tests of quality and strength are needed.

So long as the solution will yield any active oxygen at all, it will give this off with active effervescence when poured onto a crystal or two of potassium permanganate. A solution containing only a quarter of its volume will give an effervescence so strong as to be misleading and therefore a quantitative test is needed. The following is a modification of a testing process given to the writer, with much other useful information, by Mr. Charles Marchand, of No. 10 West 4th St., New York City, one of the oldest and best makers of peroxide of hydrogen, and one who supplies it to all parts of the country.

The standardizing test solution is made by dissolving 1.852 grams. of potassium permanganate in distilled water and making up the measure to 500 cubic centimetres. Each cubic centimetre of this solution is equal to one volume of active oxygen when applied to one cubic centimetre of any solution of peroxide of hydrogen.

The test is made by adding to about 50 c.c. of water acidulated with five drops of sulphuric acid, a cubic centimetre of the solution of peroxide of hydrogen to be tested. Into this, with constant stirring, is dropped, from a graduated burette or pipette, the permanganate solution until the color of the permanganate ceases to be discharged. Each c.c. and fraction of a c.c. required to reach this point, indicates one volume and fraction of a volume of active oxygen that is available in the solution tested.

If this agent is to be generally used in the treatment of diphtheria, as it well deserves to be on well established principles of action, it is very important that it be freely applied in the earliest possible stages of the disease, or while it is yet local, and therefore the agent should be easily and promptly accessible in places known to physicians, and not over a mile apart throughout a city, and in hands which know the agent well, and know how to keep it from change, and to dispense it on physician's orders.

If all pharmacists should undertake to keep it—or even all the more prominent ones—it would soon share the fate of many other important medicines. Much of it would deteriorate before it could be used, and but little of it would be in a fresh condition, while if much had to be thrown away no price that the pharmacist could reasonably charge, would secure to him a proper profit on the portion sold.

OPIUM ASSAY.

FURTHER IMPROVEMENTS IN THE PROCESS.

Again this subject is resumed for the purpose of bringing the process up to the present time, in the light of what has been written and tried by the writer, and of the pretty extensive experience of the past two years.

Fortunately much interest has been awakened to the subject, and much work has been done in many parts of the world. And perhaps the most notable paper of all that have been noticed is that of Eugen Dieterich, published in the "Helfenberger Annalen, 1887," pages 36 to 79.

Many of the steps of Dieterich's process had been long ago carefully examined by this writer without acceptance, but others now advanced, in addition, were well worthy of investigation, and occasional results of these investigations have led to improvements, which it is proposed to give.

It is still maintained here that no improvements in the original design and plan of Prof. Fluckiger, have yet been made, and that all that has been done, by this writer and others, working upon this method, has been to modify, simplify and extend the working steps of the method, and show its advantages over all others yet proposed, in accuracy and uniformity of results. The modifications introduced by this writer from his long experience with the older Staples method were exactly in line with Prof. Fluckiger's design, and hence a union of the principles of the two methods was, if better than either one of them, entitled to supplant both.

The following more complete process than that given at page 965 is the result of the writer's investigations and experience up to the present time; and it eliminates the serious error in almost all previous methods, alluded to at page 1125, as pointed out by Mr. D. B. Dott and Dr. O. Hesse.

1. SAMPLING.

Every fifth lump of a case of opium,—excepting the very small lumps and every tenth lump of these,—is separated for sampling. A cone-shaped piece is cut from each of these lumps, the apex of the cone to come from near the centre of the lump. As these are cut out a small, narrow strip is cut from the side of the cone, taking about an equal proportion from its whole length so as to get a proper relation of quantity from the dry exterior to the moist centre. These strips as taken are collected together in a mass so as to lose but little moisture by drying, and the cones are returned to the lumps. After a little practice the mass of strips from each case of opium will not much exceed 25 to 30 grammes. It is rolled out into a long cylinder, the two ends doubled in to the centre, and rolled out again,—this rolling out and folding in, being repeated six times. If the opium be very moist and sticky, a gram. of powdered starch is weighed off and used to cover the surfaces of the hands and table used in the rolling, and this starch is afterward to be taken account of in weighing off the samples. Two portions, each representing 10 grams. of the opium, are then weighed off from the mass. One of these is flattened out into a thin cake, placed on a tared watch-glass and dried until it ceases to lose weight at 100°C. or 212°F. for the determination of moisture. The other is taken for the assay.

If the original mass before rolling out should not weigh less than 25 nor more than 30 grams. the rolling out may be avoided and greater accuracy be attained by simply cutting the mass in two and weighing off each half separately, drying one and assaying the other; and repeating the assay afterward on the dried portion as a check. In such case the proportions of the assay process must be changed to accord with the weight of the sample.

In no case, however thorough the rolling out and folding in may be, can a perfectly homogeneous consistence of the mass be obtained. The drier, hard ends of the strips are still easily seen and felt in the mass, and it is easy to see that they are not uniformly distributed; and from this it results that no two portions cut from such a mass will ever assay as nearly alike as two portions of powdered opium. But the difference between two such portions will rarely be greater than .2 p.c., and this is well within the limit of error of any method of opium assay.

When powdered opium is to be assayed two portions of just 10 grams. each are to be weighed off,—one for drying and the subsequent check assay, and the other for the first assay. Powdered opium should not lose over 4 p.c. in drying at 100°C. or 212°F.

2. MACERATION.

The 10 grams. of mass is pulled out and broken into thin pieces, and dropped into a flask of 200 c.c. capacity,—100 c.c. of water added,—the whole occasionally well shaken, and allowed to stand over-night. Then again well shaken.

Rubbing the mass well in a mortar with the water added little by little, was frequently tried in order to shorten the maceration. Rubbing in a beaker with a rubber-tipped stirring rod was also tried, but all kinds of rubbing is considered to be a disadvantage to the completeness and facility of the after exhaustion. The soluble morphine element of the opium is intimately distributed through the insoluble caoutchouc-like substance of the poppy juice, and rubbing seems to condense this insoluble matter and thus render the morphine more difficult to wash out. But, if the whole heterogeneous mixture is kept loose, as by shaking, with the water, the caoutchouc and resins are kept in detached particles which are more easily washed in the exhaustion. To be convinced of this it is only necessary to take a little of the exhausted residue of opium and roll it between the thumb and finger. It is thus so compacted that water will come off of it quite tasteless, when if chewed it yields much bitterness. From the nature of moist opium it therefore follows that the rapid disintegration necessary to practically complete exhaustion, is not easily accomplished, and the writer's experience is that often after much shaking and maceration over-night, some of the harder ends of the strips are still undissolved, although softened, and more shaking is needed to complete their disintegration. The difficulty of practically exhausting opium is best known to those who do it on a manufacturing scale, and there the value of thorough disintegration by prolonged maceration and agitation is always acknowledged in practice.

When powdered opium is to be assayed, the 10 grams. of powder are well shaken with 100 c.c. of water and then an hour or two of maceration is sufficient.

The sufficiency of this short maceration is shown by the comparative experiments of Dieterich, and confirmed by the experience of this writer, and therefore powdered opium can be assayed in but little more than half the time required for moist opium.

3. EXHAUSTION.

The well shaken opium mixture is carefully poured in the centre of a well wetted, tared filter of strong paper, of 12 c.m. or 4.8 inches diameter, so folded that the lower part of the cone hangs free in the funnel; that is, folded for a rather more open angle than that of the funnel used. The filtrate is received in a beaker marked at 150 c.c. and the flask and residue are well washed with water until the filtrate reaches the 150 c.c. mark. By means of a spatula the residue is returned to the flask without breaking the filter, 50 c.c. of water is added, the whole is actively shaken for five minutes, and is then returned to the filter, being carefully poured into the centre, so that in draining the residue may be of equal thickness on all sides. This second filtrate is received in a second beaker marked at 150 c.c. and the residue is percolated and washed until the filtrate reaches the mark. In both percolations a large part of the water is dropped from a pipette held at a height of 5 or 6 inches, upon the edges of the filter and surface of the residue.

When finally drained the filter and residue are pressed between folds of bibulous paper,—dried until they cease to lose weight at 100°C. or 212°F., and weighed, the weight to be stated by percentage, for insoluble residue.

If skilfully managed this exhaustion is practically complete, although the last water comes through colored, and with a bitter taste. Many schemes for shortening this exhaustion have been tried in comparison with this method, but without success. And all the proposed methods of taking an aliquot part of a strong filtrate to represent an aliquot part of the opium have also been tried, occasionally with a fair degree of success, but in most cases with results so at variance among themselves that they were simply inadmissible. Why they are so widely at variance is easily understood by any one of large experience with various lots of opium. The proposed method of taking an aliquot part to represent the opium is based upon the assumption that opium is fairly uniform in the proportion which is soluble in cold water, and most authors, as for example Fluckiger and Dieterich, assume that this proportion is about 60 p.c., leaving an insoluble residue of about 40 p.c. Here is probably where the chief element of error lies, since in looking back over the last 11 assays of as many lots of opium, made by this writer, the insoluble residues (dropping fractions) have weighed 42, 34, 28, 36, 23, 33, 34, 27, 41, 31 and 25 p.c. This consideration alone is sufficient, on principle, to invalidate any method by which an aliquot part of filtrate is assumed to represent an aliquot part of the opium taken.

4. EVAPORATION OF THE SOLUTION.

The weaker solution is evaporated first, in a tared capsule of 250 c.c. capacity, on a water bath to about 10 c.c. The stronger solution is then added to this and the evaporation continued until the whole is reduced to 14 grams. This is rinsed round the capsule by a rotary motion until all the rings of extract formed during the evaporation are dissolved, and it is then poured into a tared flask of 100 c.c. capacity. The capsule is then rinsed into the flask with three rinsings of about 2 c.c. of water each time, and finally with enough water in addition to make the entire solution in the flask weigh 20 grams.

All the published methods of assay up to the writer's method, published in 1882 (see Ephemeris, p. 14), precipitate the morphine from a too dilute solution, and perhaps the most important modification introduced into the process by this writer is the precipitation from a concentrated solution. The mother liquor from which the precipitation is made has a somewhat variable solvent power for morphine, and this solvent power is greater for morphine in the nascent condition than for morphine added to it, and is greater than that of a clean solution of water and alcohol made to represent the mother liquor. And, all the morphine thus held in solution by the mother liquor is lost to the assay process. It therefore follows that in proportion as the volume of this mother liquor is greater, the loss of morphine by it is also greater. It is also true that if the concentration be carried too far, the process is vitiated by the precipitation with the morphine, of an undue proportion of coloring matter, etc., which it is desirable to avoid, and hence the necessity for a close limitation of this step of the process. In the weaker opiums the concentration may be safely carried to 10 grams., or the weight of the opium taken, but this is the lowest safe limit within the writer's experience; while for rich opiums 15 or 16 grams. appears to be the upper limit. Recent comparative trials have, however, shown that 13 to 14 grams. is best for the large class of market opiums and equally adapted to all which come within the range of 9 to 16 p.c. of morphine,—that is, the total watery solution for precipitation should be just 20 grams. from 10 grams. of opium. The crystallized morphine is then fairly clean and the coloring matters and other impurities, that are finally weighed with it as morphine, do not more than counterbalance the loss of morphine in the mother liquor, and by the washings.

5. PRECIPITATION.

To the 20 grams. of concentrated solution is then added half its weight, or 10 grams. of alcohol of not less than 91 p.c., s.g. .815, and the mixture is well shaken. Then 25 c.c. or 17.5 grams. of ether of not less than 93 p.c., s.g. .725, is added, and the mixture again well shaken. To this 3.5 grams. or 3.5 c.c. of water of ammonia of 10 p.c. strength, s.g. .960, is added, and the mixture is vigorously shaken for 10 minutes. Usually within two minutes from the commencement of this shaking out of the morphine,—and often within one minute, a sudden change in the sound of the shaken mixture occurs. From a soft, rather oily sound the change is to a sharp rattle; and, coincident with this change a very large proportion of the morphine instantly crystallizes out in crystals as large as the particles of fine sand. At the end of the 10 minutes' shaking the flask is set aside over-night, or for not less than 6 hours.

The additions of alcohol and ether are most conveniently made on a scale, the ammonia being added by measure from a graduated pipette. After the shaking a large part of the morphine floats between the dense solution and the ether, but after 4 or 5 hours a film begins to form on the bottom of the flask, and this increases up to 6 or 7 hours, and is not surely complete under 8 or 10 hours. With the hope of shortening this step of the process comparative trials were made in which the crystals, from a 15.09 p.c. opium were filtered out at the end of the shaking,—at 1 hour, 2 hours, 3 hours and 4 hours after, the results being compared with a pair of parallel assays which stood over-night. The first was some 2 p.c. short. That which stood 1 hour was .334 p.c. short,—2 hours, .258 p.c. short,—3 hours, .219 p.c. short,—4 hours, .104 p.c. short. But these results were all from the same powdered opium. Rougher observations with another powdered opium of lower grade, 14.24 p.c., indicated rather different results, showing that the safer practice was to allow the flask to stand over-night.

The chief difference between the precipitation from a concentrated solution of 15 grams. and one of 20 grams. appears to be, not in the crystals shaken out, but in the precipitate which afterward collects on the bottom of the flask by standing. This precipitate when from a 15 gram. solution is quite large and is never all of it soluble in lime-water. When from a 20 gram. solution it is smaller and is frequently all soluble in lime-water.

Dieterich strongly objects to the use of alcohol either in the exhaustion of opium or in the solution from which the morphine is precipitated, and his objections are experimentally demonstrated to be sound. But then he precipitated from so large a volume of liquid as to vitiate his conclusions if applied to small volumes of liquid. He precipitated the morphine from solutions weighing 5, 6, 7, 8 and 10 times the weight of the opium and gets his best results from a solution of 8 times the weight. Thus he prefers a solution of 80 grams. for precipitation, while this writer prefers one of 20 grams., and it will easily be seen that the presence of alcohol in these two solutions, will have a very different bearing upon the results. Dieterich shows that the presence of excess of ammonia within certain pretty wide limits, has no practical effect upon the results, but this showing must also be taken in connection with his large volumes of solution, as the results may not be the same with smaller volumes.

The use of alcohol by this writer in the solution to be precipitated is for the purpose of preventing the precipitation of coloring matter and other substances which would contaminate the morphine and be difficult to wash out, and that it does this, is beyond question. The question is, as to the proportion of the morphine which it retains unprecipitated in the mother liquor. Some years ago, a writer on this subject, probably P. Carles, showed that a watery liquid containing about 33 p.c. of alcohol had a very low solvent power for morphine, and upon this result the proportion of alcohol here used is based. But although this is the actual proportion of alcohol added, it must be remembered that over 10 p.c. of this is washed out by the ether, and is replaced in the solution by about 5 p.c. of ether in which morphine is practically insoluble.

6. SEPARATION AND WASHING.

The ether layer is poured off as closely as possible, and 20 c.c. of fresh ether is added to the contents of the flask, and rinsed round without shaking. This is poured off as closely as possible, and 20 c.c. more of fresh ether added,—rinsed round and poured off as before,—and this is repeated with a third portion of 20 c.c. of fresh ether. A pair of counterbalanced filters 9 c.m. or 3.6 inches in diameter, folded at an angle slightly wider than the funnel, and well wetted with ether, then receive the contents of the flask, the upper ether layer being slowly poured in first so that it may pass through before the paper becomes wetted with the watery solution. When the liquid has nearly drained through from the crystals on the filters, those from the flask are washed out onto the filters by repeated portions of water, about 3 c.c. at a time, until all the crystals are upon the filters. Then water is applied drop by drop, from a pipette held 3 or 4 inches above the funnel, to the edges of the filters and surface of the crystals until they are fairly clean and the mother liquor and washings together do not exceed 50 c.c. Then 5 c.c. of a saturated solution of morphine in 91 p.c. alcohol is dropped from a pipette first upon the crystals on the point of the filter and then upon the edges of the filters, so as to displace all the watery solution and leave them saturated with the alcoholic liquid. Then before this has time to dry it is displaced by dropping on, in the same way, 5 c.c. or more of ether. When this has drained through, the filters are closed together upon the crystals, in the original folds, and pressed between folds of bibulous paper, under weights, for half an hour. The filters are then opened, and when the morphine is spread out upon the inner one they are dried at 60°C. or 140°F. until they cease to lose weight. This is the crude morphine, and if a small portion of it is found to be entirely and quickly soluble in one hundred times (or more) its weight of lime-water, the weight of the morphine multipled by 10 is accepted as the percentage of morphine yielded by the opium.

The profuse use of ether by decantation is the easiest and best way to get rid of the original ethereal liquid which holds the narcotine, resins, fats, etc., precipitated by the ammonia, and the time and trouble saved by this decantation process very far overbalances the expenditure of ether and gives far cleaner and better results than the separation and washing with less ether by filtration. But the repeated applications of ether must be carefully managed if they are to succeed, as they should, in removing all but about $\frac{1}{1000}$ part of the original ethereal solution of the confusing impurities. If they be shaken with the solution an emulsion is the sure result, and after this the filtration and washing is very tedious and unsatisfactory, and the assay is really spoiled. If much agitated, large drops of ether become entangled with the watery solution, and these do not pass through the filters after they have become wetted with the watery solution, but dry from the surfaces of the liquid and filters, leaving the matters held in solution to vitiate the results more or less in the final weighing. Rinsing each fresh portion of ether round upon the surface and floating crystals, by a circular horizontal motion is all that is necessary or permissible. With care the pouring off can be easily done to within 4 c.c. each time, and half of the last 4 c.c. can be passed through the ether-wet filters before they become impervious to ether by becoming wet from the watery solution, so that in this way practically the whole of the ether-soluble impurities are got rid of. The few crystals which remain in the flask and which are to be washed out onto the filters, are best managed by holding the flask in an inclined position and dropping the water slowly from some height upon the inside of the neck, turning the flask slowly round during the dropping. This washes the crystals from the sides down to the bottom and gets them together. Then if they be kept loose, and in partial suspension by a slight to and fro motion while the flask is turned up over the filters, they may be nearly all tilted suddenly out with the water. Two or three repetitions of this management with about 3 c.c. of water each time will commonly get all but a very few small crystals onto the filter, especially if the straight-sided Erlenmeyer flask be used. These successive douches of water serve to wash the mass of crystals in the point of the filters pretty clean, and it only remains to wash the filters; and, if these have not been allowed to dry this is easily done by slow dropping of water from a height round and round upon the edges and folds of the paper, until the paper is of a uniform light brown tint of about the depth of the crystals or lighter. The morphine is now in a condition to be dried and weighed, and it may be dried in a few hours to an anhydrous condition by subjecting it to a temperature of 110°C. or 230°F. until it ceases to lose weight, and then adding 7 p.c. to the weight for the water of hydration or of crystallization, which has all been driven off. The percentage of anhydrous morphine might be stated, but as all authorities give and require the results in crystallized or hydrated morphine, this would be confusing and would lead to misapprehension. The crystalline condition can be preserved by drying at temperatures not exceeding 60°C. or 140°F., but when crystals and filters are water-wet as at the end of the water washing, this requires a long time, and they do not cease to lose weight at this temperature in less than 24 hours; and are liable to go back and forth in changeable or damp weather. It is, therefore, better to displace the water in the filters and crystals by more volatile liquids in which the morphine is not soluble. The use of ether for this purpose naturally suggested itself to Mr. C. M. Stillwell, but ether will not displace water easily, and so it is better to displace the water first with an alcoholic solution of morphine, as Mr. Stillwell did, after Mr. E. F. Teschemacher, Jr. This alcoholic solution is made as follows:

The morphine from one or two assays is put into a bottle of 100 c.c. capacity, and the bottle filled to three-fourths its capacity with 91 p.c. alcohol,—is actively shaken until the alcohol is saturated. When the excess of morphine settles out the clear solution is ready for use.

Of this solution 5 c.c. is enough to displace all the water if used as directed, and more than this should not be used, because it rapidly dries from the inside filter, but not from the outside one against the glass, and this drying leaves the morphine which it held in solution mainly upon the inside filter to be weighed as if belonging to the assay. As the mass of crystals in the point of the filter holds most of the water and the part most difficult to displace perfectly, the first c.c. or two of the alcoholic solution is dropped upon these crystals. Then the remainder is dropped upon the edges and folds of the filters. This is immediately followed by the 5 c.c. of ether applied in exactly the same way, and it pretty thoroughly displaces the alcohol. But should there be any doubt about the thoroughness of this displacement, another 5 c.c. of ether may be used, since there is no risk of vitiating the results with ether. The drying of the morphine at 60° C. is now rapid and easy, being usually complete in about two hours.

For some months past some of the opium assays, that have come under the supervision of the writer, have been done in triplicate by himself and two assistants,—two being managed as here described and one being managed by Mr. Stillwell's method of washing with morphiated water and morphiated spirit, as originally recommended by Mr. E. F. Teschemacher, Jr. The general result of these comparisons was, that when everything else was equal the percentage of morphine did not vary more between those washed with morphiated solutions and those washed with water than between the pair washed with water. The differences were rarely greater than .2 p.c. and never greater than .3 p.c., each method giving lower results quite as often as higher. Now as these results are within the limits of error claimed for the accuracy of this method of assay, it is submitted that the refinement by the use of morphiated washings is worse than useless for general practice.

7. CORRECTION OR CONTROL OF RESULTS.

When the preliminary testing of a small quantity of the precipitate shows that it is not all entirely soluble in lime-water, .5 gram. is weighed off,—put into a graduated cylinder and 50 c.c. of lime-water is added, by pouring down the side of the inclined cylinder. The contents of the cylinder are then tilted backward and forward without shaking, so as to avoid the formation of froth on the surface, until all that is soluble is dissolved. Whenever there be doubt as to when the solvent action is complete or not, the agitation is continued until the undissolved particles cease to diminish in size or number. The solution is then filtered through a pair of counterbalanced filters about 7 c.m. or 2.8 inches in diameter, and the filters and residue are well washed first with 5 c.c. of lime-water and then with 5 c.c. of water, and when drained they are closed up, pressed between folds of bibulous paper, dried until they cease to lose weight at 100° C. and weighed. Then as .5 gram. of the crude morphine is to the weight of this residue, so is the weight of all the crude morphine to the total amount of insoluble residue it would have yielded, if the whole had been subjected to the action of 100 times its weight of lime-water. The weight thus obtained subtracted from the total weight of crude morphine gives the net weight of pure morphine; and this multiplied by 10 gives the corrected percentage.

It almost always occurs that there is a very small proportion of the precipitate that is insoluble in lime-water, although it may or may not be visible until the cylinder be left at rest for half an hour or so. Such residues when filtered out are generally found to weigh only 1 to 3 milligrammes, and as each milligramme of residue is equal to only about .03 p.c., such residues may be neglected.

The crude morphine, subjected to the action of the lime-water, need not be powdered, since the crystals are easily and rapidly dissolved, but it is important that the whole precipitate should be well mixed before the .5 gram. is weighed off from it, and that by pressure with a spatula all lumps should be broken down to the general size of the crystals. In proportion as this is effectively done the action of the lime-water will be prompt. When by pouring the lime-water onto the morphine at the bottom of the cylinder or by shaking, a froth is produced, this is liable to entangle particles of residue or undissolved morphine sufficient to slightly vitiate the correction, while the froth always interferes more or less with the filtration, because when once formed it never breaks down. But it is always easily avoided by the management directed.

8. TITRATION OF MORPHINE.

Mr. D. B. Dott (see *Pharm. Journ. and Trans.* for February 25, 1888, p. 701), gives as the formula for crystallized morphine $8C_{17}H_{19}NO_3 9H_2O$. This gives a combining weight of 305.25. The formula as given by all other authorities known, is $C_{17}H_{19}NO_3H_2O$, which gives 303 as the combining weight. By calculation from Mr Dott's formula .5 gram. of morphine requires 16.38 c.c. of decinormal solution of oxalic acid for saturation. From the more generally received formula 16.5 c.c. are required. By actual experiment 55 c.c. of lime-water require 22 c.c. of the decinormal oxalic acid, and phenolphthalein is a very sharp indicator of the saturation point with lime-water, but is without effect in the saturation of morphine, and hence the following method of titration.

The lime-water solution of .5 gram. of morphine and washings are tinted with 10 drops of solution of phenolphthalein, and decinormal solution of oxalic acid is dropped in from a burette until the color is discharged. The amount of oxalic acid required indicates the amount of lime-water present in the proportion of 40 c.c. of the decinormal oxalic acid to 100 c.c. of lime-water. The burette is then refilled to the 0 mark for the saturation of the morphine present, and the oxalic acid is dropped in until neutral litmus paper is just slightly reddened. The quantity of the decinormal oxalic acid required should not be less than 16.4 c.c., which indicates, according to a molecular weight of 305.25 for morphine, a degree of purity equal to 100 p.c.,—or, according to a molecular weight of 303, 99.4 p.c. These figures and results will of course apply only to those assays wherein there are no residues insoluble in lime-water. Whenever a correction has to be made, of course the titration applies, not to .5 gram. of morphine, but to .5 gram., less the correction, and then the decinormal solution required will be proportionately less.

This titration to be fairly successful requires very close and careful work with the litmus paper indicator. Ordinary deep blue litmus paper gives too high an indication for the morphine. But well made neutral or purple paper gives a fairly sharp indication if one end of the strip be wetted with distilled water to the same extent that the other end is wetted by the solution to be tested. The purple that becomes faintly more red at one end than the other can then be seen. If the burette be read off and noted at this point, and then a few drops more be used to very distinct acidity, the excess of acid may be titrated back with decinormal sodium solution, and as a farther check the sodium solution may be continued back to the restoration of the phenolphthalein red color.

Many trials of this method of titration have been made, and the results have always been negative. That is, no deficiency of morphine has been found in the results of the assays. Indeed the actual titrations occasionally went above the calculated figures.

In general practice, perhaps 19 times out of 20 the lime-water testing will show an insignificant amount of insoluble residue, and then the assay process may well end there as far as its general practical value goes, and the correction and control of results; and the titration is merely held in reserve for exceptional cases, and unusual varieties of opium.

In comparing the above method of assay with those given at pages 14, 695, and 1113, many changes of detail will be noticed, and many of these are of much importance. And again, many details and explanations are given in one paper that are not alluded to in others, so that reference should be made from one to the other upon points that are not clear in the later papers.

BOSTON OPIUM.

A short note at page 1127 of the last number of this series of pamphlets drew attention to this then new variety of opium in this country. Since that time it has become very popular with brokers and jobbers, and its popularity is rapidly extending to the retailers, and in every direction, excepting, only, among that class of consumers who use opium as a vice,—and those who supply that class of buyers. The writer asked his correspondents in the original opium markets to get for him what information they could upon this opium, with the following results.

It seems to be entirely a mercantile enterprise suggested by, and based upon the U. S. drug law, which forbids the importation into this country of any opium that contains less than 9 p.c. of morphine, and its inception and origin were in a well-known Boston house, of very high mercantile standing. The order was, substantially, to take the natural opium of good quality and reduce the strength by adulteration with foreign matters until it would just pass the assay process of the U. S. Custom Houses. The Turkish agents,—who are as well known as their principals,—found that by skilful manipulation in doing this, a very handsome opium of uniform consistence could be easily made, and this could be as easily divided into handsome lumps of uniform size. Then, the skill to use the poppy leaf as an envelope being indigenous, a very handsome result could be easily and cheaply attained, for the rapidly increasing demand of the markets of this country. This enterprise has been so very successful that now, within the short time of two years, the markets are literally flooded with this Boston opium, or, "Pudding Opium," as it is sometimes called. The plausible reason for this is not difficult to find. A buyer whose first,—and often whose only—interest is pecuniary profit, sees a case of Boston opium and a case of natural opium opened side by side, and finds a difference in price of about 15c. per pound in favor of the Boston opium, whilst the difference in appearance is far greater. The lumps of Boston opium are regular in size, shape, consistence, etc., while the natural opium is of many sizes, shapes and consistence, and much less attractive looking,—the one, say, at $3.40, the other at $3.55 per pound. If in appearance they were equal, the price would decide the purchase. But when price and appearance are both on one side there is rarely much hesitation in the drug market. Under these conditions it is not surprising that Boston opium in this short time has gone all over the land. The very best houses known to the writer deal in it, and it pleases everybody excepting only those who consume it as a vice, who are the most critical buyers. And, this class being very large, a market for natural opium is still kept up. So attractive is Boston opium, that pharmacists who have had it from their wholesale houses, and have afterward been supplied with natural opium, have sent the latter back under a charge of inferiority, demanding more honest treatment. Now the facts upon which this condition of things is based, are, that this Boston opium is fictitiously made to contain as nearly 9 p.c. of morphine as is easily practicable, and at $3.40 per pound each per cent. costs (3.40 ÷9=) 37.7 cents. Natural opium can be had that will yield from 9 to 14 p.c. of morphine, according to price. But that which brings about 15c. per pound more than Boston opium contains about 11.5 p.c. of morphine. Then $3.55 for 11.5 p.c. opium costs (3.55÷11.5=) 31c. for each per cent., and therefore if the true intrinsic value of Boston opium be $3.40 per pound, that of a natural opium containing 11.5 p.c. of morphine would be $4.34 per pound. The difference in price is 15c., while the difference in actual value is 94c. That is, the buyer pays (94—15=) 79c. per pound for appearance against actual value. And this is well known, but the buyer says, with fine sarcasm, that he is afraid of poisoning somebody with this strong opium.

SPECIFIC GRAVITIES OF LIQUIDS.

The subject of specific gravities is resumed here from pages 204, 349 and 529 for the purpose of showing a new and convenient, as well as more accurate form of apparatus. It is well known that the standard volume of water for unity in comparing, varies in different nations and under different circumstances. In continental Europe generally the volume of water at its maximum density of 4°C. or 39.2° F. is the common standard.

In Great Britain this standard is not uncommon, though by no means universal, two other standards being in common use; namely, 62°F. or 16.667°C. and 60°F. or 15.556°,—usually taken as 15.6°C. In this country all these standard volumes are in use, although 62° F. is only used when needed in connection with the older British recorded usage. To these the U. S. Pharmacopœia has added another standard volume; namely, 15°C. or 59°F.

This multiplicity of standard volumes is rendered still more confusing by the very common omission to state what standard is used when specific gravities are given. Three ways of giving specific gravities are in common use. The most common of all is to give the figures without temperature, as for example, s.g. 1.256,—and what this really means no one can tell. When used by an European authority of known scientific accuracy it should mean s.g. 1.256 weighed at 4°C., and compared with an equal volume of water at the same temperature. This is a true specific gravity, but a troublesome one to take, requiring time and skill and ice, even with the best form of apparatus.

The way of giving specific gravities which is perhaps next in frequency, is to write s.g. 1.256 at 15.6°C. or 60°F. Here the temperature at which the liquid is weighed is clear, but the reader is left in doubt in regard to the standard volume. If this was an equal volume of water at the same temperature as the liquid with which it was compared, then this is a true specific gravity. But if it was an equal volume of water at any other temperature, then it is not a true, but an apparent specific gravity, and is misleading.

The third, and perhaps the least frequent way of giving specific gravities, is the only correct way, and that is to write s.g. 1.256 at 15.6°C. compared with water at the same temperature. This for true specific gravities;—or, compared with water at 4°C., or at any other stated temperature if for apparent specific gravities.

Again, this writer many years ago proposed a new temperature for specific gravities; namely, 25°C. or 77°F., compared with water at the same temperature, to the end that they might be much more easily and more quickly taken at all times of the year and without ice. And he proposed that such specific gravities should be given in addition to those at the more common temperature of 15.6°C. This method has been adopted often enough to demonstrate its great utility, and the Pharmacopœia has adopted it in a few cases. In such a book it would be most convenient in all cases, because by the economy in time and trouble the testing of liquids by s.g. would be much more frequently practised.

The ordinary specific gravity bottles sold by the apparatus dealers are all adjusted to a single standard volume with varying degrees of accuracy, but very few of them accurate enough for the close work that is now so often required. Beside being available for comparison for only one standard volume, their general defects are first, that they are adjusted too soon after being made, and as glass contracts considerably for a year after it is blown, and to a diminishing extent for some time longer, they are for this reason often too small, and give results that are too low. And, second, that very few of them are provided with any means by which the liquid can expand without loss during the weighing. The ordinary bottle, with or without a capillary channel in the stopper, cannot be weighed without loss in a room which is above the temperature of the liquid at the time of filling.

To accommodate the two most common standards of temperature; namely, 4°C. and 15.6°C.,—and this new one of 25°C., bottles with three capacity marks, have for many years been in use by the writer, and such a bottle is shown at page 529.

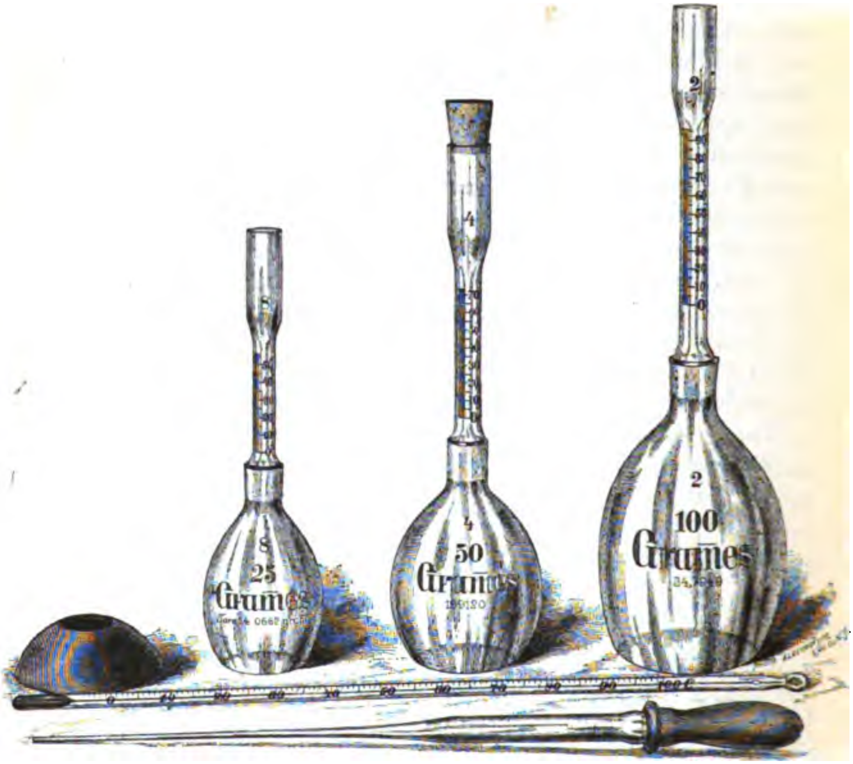
And, still farther to improve this bottle the writer has had made by Mr. Emil Greiner, of No. 63 Maiden Lane, New York, N. Y., a set of bottles, as shown in the following cut, wherein the tube stopper is lengthened out so that the central channel will permit the bottle to hold the volume of water at any temperature between 4° and 25°C., thus adapting it to all the standards in use. The tube between these points is graduated to half millimetres or less, and at the top, above the scale, it is expanded so as to allow room for the expansion of light liquids, without loss, when the bottle is adjusted at 4°C., and weighed at higher temperatures, the expanded portion being loosely closed with a cork during the interval of warming between the adjusting and the weighing, this cork being removed, of course, during the weighing.

In constructing this bottle the stopper is ground off until the bottle and tube hold the standard weight of recently boiled distilled water at 4°C. up to about the point where the scale is to begin. Then the stopper is ground very fine so that the bottle when filled to the top of the tube does not lose weight in 4 hours' standing. The standard weight of boiled water is then again put into the bottle, and the bottle and water are cooled in a bath to 4°C. until the water in the tube remains stationary. The lower limb of the meniscus in the tube is then marked at this point for the beginning of the scale. The bath is then warmed up to 25°C. and held there until the water column in the tube ceases to rise, and this point is marked for the upper limit of the scale. The tube is then graduated in half millimetres from 0 to 25°C., allowing the graduation to run up a few marks above the 25°C. point. The tube is then cut off just above the scale, and the enlarged upper portion into which liquids are to expand during warming, is fused on. The bottle and stopper are then numbered to keep them together, and the capacity mark is put on. Bottle and stopper are then made chemically clean by concentrated sulphuric acid, water, alcohol and ether rinsings, in the order named, and when perfectly dry and cold are tared on a fine balance to the fourth decimal place, and this tare is etched on the bottle under the capacity weight. Although when skilfully ground the stopper is quite tight, even to such liquids as ether, the putting in and taking out are much facilitated by a light coat of soft paraffin upon the ground surfaces. Such a coat adds about one milligramme to the tare,—so little that in ordinary work it is disregarded.

The accompanying cut sufficiently illustrates the bottle of the three sizes that are commonly needed; and shows beside, a leaden collar that goes over the neck of the bottle to keep it steady in the bath, a thermometer for the bath, and a fine pipette with rubber nipple that is useful in a coarse adjustment of the liquid to the mark. The fine adjustment is more conveniently made with a narrow strip of blotting paper.

These bottles are always used in a bath, and there need be no internal thermometer, because the bottle itself is but a thermometer, which, by means of the bath, is to be compared with the thermometer used in the bath to adjust by.

In consequence of the contraction which occurs in glass during the first year or two after it has been heated, every close observation made with any given bottle which is not known to be two years old, or more, since it was heated, should be preceded by a verification of the bottle, and such verification of these bottles is simple and easy. For example, the 100 gram. bottle has weighed into it at room temperature exactly 100 grams. of distilled water recently boiled and cooled. It is then loosely corked, loaded with the leaden collar and set in a bath of water which has in it a good sensitive chemical



Specific Gravity Bottles for Various Standards of Volume.

thermometer of known error. Suppose the specific gravity is to be taken at 4°C. Plenty of ice is put into the water of the bath and the whole is well stirred until the thermometer indicates about 3° C. After it has been held at this temperature until the column in the tube of the bottle has ceased to move as watched by the graduation marks, the ice is taken out and the bath is adjusted accurately to 4°C. and held there by small additions of ice water for a few minutes. For a degree or more on each side of this temperature water does not change in volume enough to be seen in this apparatus, but the bottle itself changes much more in its capacity, and therefore it is for the bottle rather than for the water, that the final adjustment of temperature is to be accurately made. The meniscus in the tube is then closely read off by the graduation and noted. If the zero mark of the scale was correctly placed for 4°C. when the bottle was first made, and if the verification was made some months after, the reading will be above the original zero mark in proportion to the age of the bottle, until the contraction has altogether ceased, and the amount of the contraction will vary with the composition of the glass, and with its thickness. But whatever the amount of the change may be, it is now easily read by the graduations of the scale, and that reading, whatever it may be, will be the standard volume at 4°C. until the next verification, and the readings for the different standard volume temperatures will be carefully kept in some note book. The record for the several standards will of course be kept in the terms of the scale. That is, for example, 2 divisions of the scale may be the point for 4°C., while 30 may be the point for 15.6°C., and so on throughout, for any temperature volume.

The bottle having been recently verified, accurate specific gravities are quickly and easily taken, the volume of liquid being always adjusted while the bottle is in the bath at the proper temperature, after the column in the tube has not moved one division of the scale in five minutes. It is, however, always necessary to keep the bath well stirred from the lower to the upper strata, especially during the time when it is held at the standard temperature, just before the final adjustment with the strip of blotting paper.

CRUDE COCAINE.

It seems highly probable that the importation of coca leaves into this country and Europe for the manufacture of cocaine is nearly at an end. For more than a year past crude or raw cocaine has been sent from Peru to this country and to Europe in rapidly increasing quantities, and of better and better quality. In October, 1885, the first considerable parcels of crude cocaine were examined by the writer, and for a year and a half after this, it came in small lots and of poor quality, often containing only 50 to 60 p.c. of alkaloid, and this in a condition difficult to purify.

During 1887, the quantity increased and the quality improved very much, but chiefly during 1888 the quantities exported from Peru became very large and the quality reached 90 to 96 p.c., and occasionally even 98 p.c. There are now at least four manufacturers in Peru, and two of these who make the largest quantities of the best cocaine have recently been in this country and in Europe. These are the firms of C. M. Schroeder & Co., and J. Meyer, and from them much important information was obtained.

It was a great satisfaction to this writer to learn that the early publications of his processes in this Ephemeris were the starting point of this industry in Peru, and that these processes, used with increasing experience and skill, are still worked, and yield the now very large output. The two largest makers are Germans, and the chief market for their products is Hamburg; and, curiously enough, their products can be had here better, cheaper and in a shorter time from Hamburg than from Peru. Beside this, there is a combination of the makers now to keep up the price and to confine the sales to Hamburg. Some idea of the very large quantities produced may be had from the circumstance that one maker has a single contract with a European house for 70 kilogrammes or about 154 pounds per month. Another curious circumstance connected with this young industry is that one of the largest and most successful makers is by trade, and was by occupation, a bricklayer when these processes were published, and simply took them up as a better and more promising trade for making money.

The advantages of exporting the crude alkaloid rather than the coca leaves are many and important. As cocaine is transported in the treasure chests of the steamers the difference in freight is about as ½ lb. to 100 lbs. of the leaves. But a much more important economy is shown by a comparison of the yield of alkaloid, by the same process from the same leaves, as worked here and in Peru,—the yield there being 13 to 15 p.c. greater. This is easily accounted for by the circumstance that in their very moist climate it is practically impossible to pack the bales of leaves so dry that they will not heat in transportation ; and this heating destroys a part of the alkaloid or changes it into other alkaloids, etc., just as heat in the process of manufacture will do. Beside, there the leaves are manufactured while in their best and freshest condition. Again the cost of the leaves is very much less in Peru, and very much more uniformly low, while speculation in them is largely avoided, —the cocaine being less liable to speculation. Although labor is much lower in wages there than here, it is of so much lower quality that the difference in cost is not great, and what difference there is, is in favor of this country. The great disadvantage to this country is the 25 p.c. ad valorem tariff duty on the alkaloid imported, while the leaves are free, yet this does not counterbalance the advantages, but only makes the people here pay 25 p.c. more for the relief of their suffering than they need pay, or than the people of European countries do pay, while it really does not benefit the three or four manufacturers who import their crude cocaine.

It is therefore a protective duty which does not protect, but merely taxes the consumer. That is, the crude cocaine can be imported so much cheaper than it can be made here that the duty is paid, and then the price of the salt here is reduced 25 p.c. below what it was when made in this country from the leaves, and at quite as good a profit when the greatly reduced expense of manufacture is considered.

This crude cocaine comes either in granular powder or in fragments of press cake of all sizes and forms up to an inch or two in superficial area, and of a thickness of cake from a quarter of an inch to an inch, with some small fragments and powder from attrition, and the sides of the fragments have the print of the press cloths. The general color of these fragments is a dull, creamy white, but is rarely quite uniform throughout any package, varying from a dirty or brownish white to very nearly white. But, in this matter of color it is constantly improving. The fragments vary more in consistence than in color. A large proportion are hard, compact and slightly horny when cut or scraped, while others are softer, more porous and chalk-like, and easily cut or scraped,—the general density being lighter than the softest, lightest chalk.

The differences in color and density denote differences in purity. Hence, as different fragments of the same parcel give results by assay which occasionally differ as much as 5 p.c., the sampling for an average assay must take portions from a great many of the fragments. The parcels generally contain from 2 to 6 p.c. of moisture, and it is probable that on this account they do not bear to be closely shut up as in tin boxes without acquiring a bad odor, and undergoing some decomposition; whilst when they are not so shut up they constantly lose in weight. At present the improved practice is to put the broken cakes into muslin bags which hold about 5 kilogrammes each, the strings with which the bags are tied being often sealed. These bags are commonly packed either two or four in a light wooden box, and are so transported in the treasure chests of steamers.

The crude cocaine is usually sold at so many German marks, or U. S. dollars per kilogramme of 100 p.c. purity, the Peruvian currency being generally ignored on account of its variability in value. Some 6 months ago the average price of 20 kilo. lots of the best kinds, in Hamburg, was about 600 marks or $138.00 per kilo. Now (June, 1889,) it is about 480 marks or $113.00, to which for this country, freight insurance, 25 p.c. duty and Custom House expenses have to be added.

In Hamburg it is nearly or quite all sold upon the assay of Dr. Gilbert, and the results of this writer have generally been in fair accord with those of Dr. Gilbert, and the New York Custom House has generally accepted his results in adjusting the duty. But as Dr. Gilbert has never made his assay process known, and as the subject is daily increasing in importance, it is the chief object of the present note to publish the assay process of the writer.

This is a simple and easy process requiring about two hours,—or with the sampling about two and a half hours, and the results have been confirmed by experience in the manufacture of many parcels assayed by it.

ASSAY OF CRUDE COCAINE.

The contents of a bag being emptied into one side of a large vessel, fragments of the cake are freshly broken, and small portions are cut or scraped off from the fresh fracture into a wide mouth vial, corked to prevent drying, and thus carried to the laboratory. An hundred or more pieces should be thus sampled and laid on the empty side of the vessel to avoid sampling the same pieces more than once, and a little of the coarse and fine powder that is found in every bag, rubbed off by attrition, should be added to the samples.

The aggregate sample is thoroughly mixed and rubbed to fine powder in a mortar, and then the three portions are weighed off for assay, and the remainder corked up in the vial and returned to the owner with the results of the assay.

To determine roughly the proportion of other alkaloids present .5 gram. of the powder and 2 c.c. of strong hydrochloric acid are put into a small test tube and carefully warmed over a gas flame until the decomposition is complete as indicated by the end of the effervescence, and the commencement of boiling. Perfectly pure cocaine, or hydrochlorate of cocaine, when thus treated yields an almost colorless solution, and the depth of color indicates the amount of impurity. The best crude cocaine yet met with gives a color of the depth of ordinary brandy, but a large proportion of the parcels give solutions many shades darker, and some of the earlier and worst specimens give black solutions. Good hydrochlorate of cocaine tested in this way gives a nearly colorless solution, or at most a pale wine tint.* On standing for a few hours these solutions give fine groups of crystals.

To determine the moisture one or two grammes of the powder are heated on a tared watch-glass to about 91°C. or 196°F. until it fuses. Then it is cooled and weighed. The loss has varied in different parcels between one and six per cent., but has rarely been above three per cent.

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* So far as yet applied this appears to be a very valuable test, and for it the writer is indebted to Dr. Ralph Stockman, of the University of Edinburgh. The following is a quotation from a private letter from Dr. Stockman to the writer, dated December 26, 1888: "I am sorry I cannot agree with you that cocaine is the only base present in the coca leaves, and that the other products are derived from it. Benzoylecgonine is so, of course, but not the others. I fancy, although I say it with deference, that isatropylcocaine is often present, in large amount, in the leaves, and I have found that the residues you sent me

To determine the alkaloid a shaking out process is used, and for this a pair of separators, such as are shown at page 786, and repeated here on the opposite page, are a very great convenience, the solutions being separated from one to the other as required, with great facility and accuracy.

In a tared beaker of about 50 c.c. capacity, with a stirring-rod also tared, 2 grams. of the sample are weighed. To this is added 12 c.c. of ether s.g. 725, at 15.6° compared with water at the same temperature, when by a minute's stirring all that is soluble is dissolved. The solution and residue are poured onto a pair of small counterbalanced filters 7 c.m. or 2¾ inches in diameter, in a funnel too large for them, placed in one of the separators. The beaker, stirrer and residue are repeatedly washed into the filter with small portions of fresh ether until they are entirely clean. The funnel, filter and residue are then also washed entirely free from alkaloid by fresh portions of ether delivered from a pipette drop by drop upon the funnel, paper and residue. This washing must be very thorough and must extend to the outside of the point of the funnel at the close. The filtered ethereal solution in the separator will then amount to about 45 or 50 c.c. The filters and contents,—and the beaker and stirrer if there be any residue adhering to them,—are dried and weighed to give the residue insoluble in ether.

To the ethereal solution in the separator 10 c.c. of normal volumetric solution of oxalic acid are added, and the whole well shaken, to shake out the alkaloid as a solution of acid oxalate. When the liquids have completely separated, the acid solution is drawn off closely into the second separator. To the ether remaining in the first separator 10 c.c. of water and 2 drops of normal solution of oxalic acid are added, and the whole well shaken together. When completely separated the lower watery solution is drawn off into the acid solution in the second separator. The ether in the first separator is again washed twice in the same way with about 3

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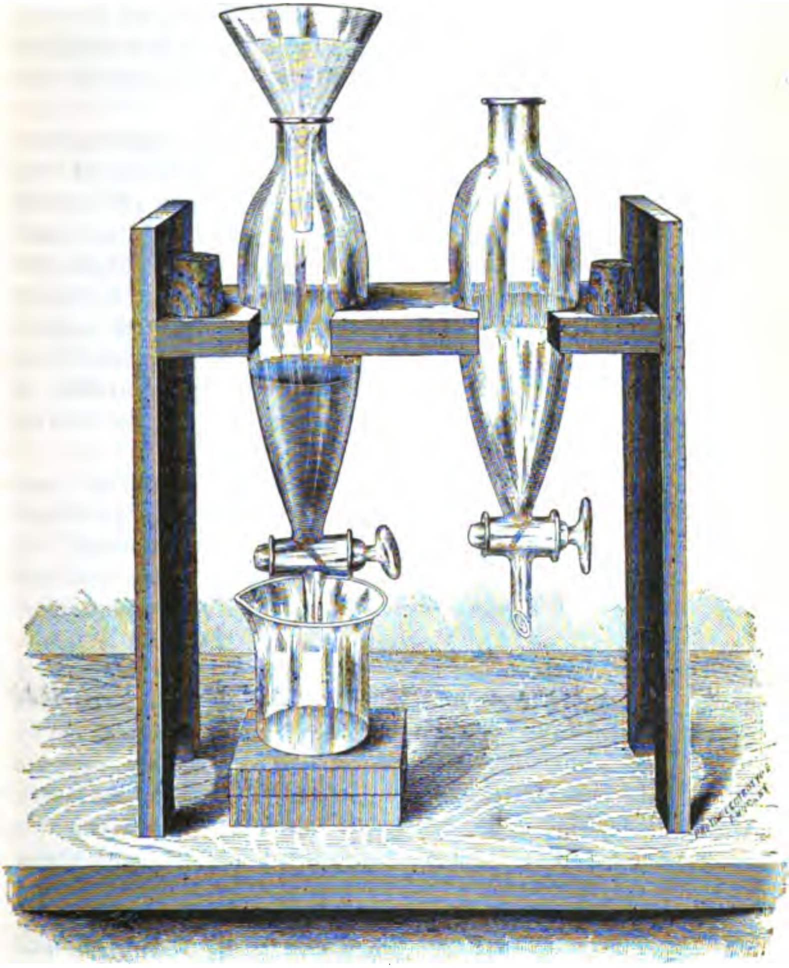
consist chiefly of this base. It may be known by dissolving only slightly in caustic soda or potash. The best test, however, is this, and I would ask you to look into it. When pure cocaine (or pure hydrochlorate of cocaine, of course) is heated with strong hydrochloric acid in a sealed glass tube in the water-bath, it splits up into its components without any change of color, except a very light yellow tint (from the HCl, I think, but perhaps from slight impurity). When isatropylcocaine is so treated, it splits up into ecgonine and a brown oily-looking body which is decomposed isatropic acid. With long boiling a black body is deposited." Upon trying this reaction the writer found, or judged, that the sealed tube and water-bath were not essential, and that the process as described above afforded very useful and critical indications in the few cases to which the test has been as yet applied.



SEPARATORS.

c.c. of water each time and the washings drawn off into the acid solution in the second separator. Then the washed ether is poured out of the top of the first separator into a tared beaker of about 100 c.c. capacity. The first separator is then well rinsed with 15 c.c. of fresh ether and 2 c.c. of water, and the whole drawn off into the second separator with the acid solution, leaving the first separator clean to become now the third separator for the next step of the process.

The acid solution and washings are now well shaken together, and after separating completely, the acid solution is drawn off into the third separator. The washing ether remaining in the second separator is then washed twice with 3 c.c. of water each time, and the washings drawn off into the acid solution in the third separator. The washed ether then remaining in the second separator is poured out of the top of the separator into the ether in the 100 c.c. beaker, and this ether is evaporated to dryness and the beaker weighed to give the impurities soluble in ether. This residue is usually in the form of a varnish hardly visible on the inside of the beaker, and is usually very small in amount.

The second separator is now well rinsed with 15 c.c. of fresh ether and 2 c.c. of water and the whole drawn at once, without separation, into the third separator, which will now contain all the acid solution of the alkaloid and 15 c.c. of fresh ether, and the second separator will be clean, to become now the fourth separator.

To the contents of the third separator are then added 10 c.c. and 3 drops of normal volumetric solution of soda, which gives 1 drop in excess of the oxalic acid solution previously used, and thus insures the complete precipitation of the alkaloid to be dissolved by the ether. The whole is well shaken, and when allowed to separate completely the lower watery solution is drawn off into the fourth separator. The ethereal solution in the third separator is washed by shaking twice with 3 c.c. of water each time, the water being drawn off into the fourth separator. The ethereal solution is then poured out of the top of the third separator so as not to get a single drop of the water with it, into a tared beaker of 50 c.c. capacity. The third separator is then rinsed by shaking in it 10 c.c. of fresh ether and 3 c.c. of water, and the whole washing is at once drawn into the fourth separator.

To the contents of the fourth separator 1 drop of normal solution of soda is added, and the whole well shaken, and allowed to separate completely. The watery liquid is then drawn off into a beaker, and having been tested to see that it is fully alkaline in reaction, it is thrown away. A few drops of water are added to the ether washing in the separator, shaken round with the ether and drawn off, and then the ether is poured out of the top of the separator into the beaker with the main portion of the ethereal solution, carefully avoiding even a single drop of water which would carry some oxalate of sodium with it.

The beaker with the ethereal solution is then set in a warm place for the spontaneous evaporation of the ether. After some hours, or over-night, the ether will have gone off and left the alkaloid crystallized, often in beautiful groups, upon the sides and bottom of the beaker. These crystals are to be dried until they cease to lose weight at 90°C. or 194°F. and are then weighed to give the percentage of alkaloid. But in the condition in which the ether leaves them they cannot be well dried. They must be broken up, or cut up with the end of a knife, into small fragments from time to time as they dry, and the finer the subdivision the sooner they reach a constant weight. In their behavior under the knife in this cutting up the purity of the alkaloid is usefully indicated. If they are brittle, and break up easily with a fracture, the alkaloid is proportionately pure and free from decomposition products or other alkaloids. If they cut toughly, without fracture, and the crystals have interstitial sticky or tough matter not well crystallized, the alkaloid is proportionately impure.

Generally all this drying process may be much shortened by at once heating the contents of the beaker until they fuse to a clear, pale, yellow, viscous liquid. This fusion occurs at about 92°C. or 198°F., and it may be done in a common drying stove or by holding the beaker for a few minutes in a bath of boiling water. The beaker and contents are then cooled and weighed. Then on standing for 24 hours this cocaine again crystallizes, with the increase of a few milligrammes in weight.

Under all circumstances, however, the alkaloid is to be submitted (after weighing) to the described modification of Dr. Stockman's test, and the color of the hydrochloric acid residue will indicate the degree of purity. And when this color is compared with that of the same testing of the crude cocaine it will always be very much lighter, while the testing in the same way of the ether soluble impurities as left in the 100 c.c. beaker will sometimes be black.

The actual process of assay requires only about 2 hours, but the drying of the alkaloid is tedious and troublesome, requiring about 24 hours. It may be accomplished in an hour by heating at 100°C. or 212°F. in a water-bath or a drying stove until it fuses. But this heating involves some decomposition and vitiates somewhat the hydrochloric acid testing.

For an approximative, but still useful assay, the first ethereal solution may be evaporated and the residue be fused and weighed as alkaloid. But this of course gives too high a result.

The results of a recent assay may be usefully given by way of illustration. The hydrochloric acid test gave a solution of a deep amber color,—or of dark brandy.

Loss of moisture on fusing	0.065			3.25	p. c.
Residue insoluble in ether	.105	gram.	or	5.25	"
Residue soluble in ether	.010	"	"	.50	"
Alkaloid, nearly pure	1.798	"	"	89.94	"
	1.978	"		98.94	p. c.
Loss	.022	"		1.06	"
	2.000	"		100.00	"

An assay made from a sample of one or two of the best cakes of this same lot gave of alkaloid 94 p.c. And another from two or three of the worst cakes gave about 78 p.c.

SPIRIT OF NITROUS ETHER.

Some thirty-three years ago, after an experience of about three years in making this preparation by the process of the U. S. P. of 1850, the writer made a partial investigation of the subject, which was published in May, 1856, in *The Amer. Journal of Pharmacy* for July, 1856, vol. xxviii., p. 289. He now decides to resume the subject after a continuous experience of nearly forty years on almost every scale of manufacture, from that of the Pharmacopœias up to 500 lbs. at a time, every two or three months.

As much of the work given in the paper referred to is pertinent to what is now to be offered; and as the principles of the improved process described have never been changed nor varied much for any considerable length of time during this long experience, it is thought to be worth while to republish that paper here, premising that the casual reader may pass it over, perhaps, without much loss.

SPIRITUS ÆTHERIS NITRICI.

By Edward R. Squibb, M. D., U. S. Navy.
Assistant Director U. S. Naval Laboratory.

The U. S. Pharmacopœia formula for this preparation is as follows:

"Take of Nitrate of Potassa, in coarse powder,	two pounds,
Sulphuric acid,	a pound and a half,
Alcohol,	nine pints and a half,
Diluted alcohol,	a pint,
Carbonate of potassa,	an ounce.

Mix the nitrate of potassa and alcohol in a large glass retort, and having gradually poured in the acid, digest with a gentle heat for two hours; then raise the heat and distill a gallon. To the distilled liquor add the diluted alcohol and carbonate of potassa, and again distill a gallon."

The apparatus necessary to conduct this process properly is as follows: A tubulated retort of a capacity of two gallons. Into the tubulure, through a perforated cork, a tube thermometer should pass, so that the bulb may be near the bottom of the retort. A Liebig's condenser of good size, and a receiving bottle marked at one gallon by slips of paper. The mouth of the bottle should be tied over with a piece of sheet caoutchouc that has been perforated to receive the eduction tube of the condenser. The connections should be made with moistened muslin, covered with sheet caoutchouc.

The mixture is made in the retort in the order of alcohol, potassa salt, and acid, and the whole shaken round. The apparatus is then set up in a steam or water bath, and the materials digested at 100° for two hours, and then heated to active distillation. The greenish yellow mixture commences to boil at 125°, and at 130° full active ebullition and distillation is established. From this point the temperature gradually, and toward the last. very slowly rises to 184°, when 5½ or 6 pints of colorless distillate will have passed over. This distillate is free from any perceptible odor of hyponitrous ether, but has throughout a distinct odor of sulphuretted hydrogen. The salt in the retort forms a cake at the bottom, and the liquid boils around and over it without any apparent effect upon it.

The distillation then slackens somewhat, but no perceptible reaction will have taken place till 6 pints of colorless and odorless (except for sulphuretted hydrogen) distillate has passed over. An hour or more is thus occupied before the period of reaction arrives. The cake then commences to dissolve and break up, the solution becomes gradually of a deeper yellow tinge, faint yellow vapors appear in the retort, the temperature rises slowly to 185° or 186°, the distillation increases, and the distillate becomes perceptibly yellow. Coincidently with these changes, and indicating distinctly the full establishment of etherification, the temperature in the retort commences to fall. When it has fallen one or two degrees the heat should be shut off and the reaction be allowed to go on spontaneously, or with only a very slight heat at most. As the temperature falls, the distillation slackens, till at 170° it only comes over by a fast dropping. If the prescribed quantity has not passed over, the heating should then be cautiously resumed, and the remainder driven over at a temperature not exceeding 180°.

If, on the contrary, the active heating should have been too long continued, and the reaction becomes too active, so that much gas and uncondensed ether vapor passes over, the heat must be entirely withdrawn and the retort cooled with water, copiously applied. This requires rapid and dexterous manipulation to avoid an undue proportion of aldehyd in the distillate; for, although aldehyd comes over at all stages of the process, it comes much more rapidly as the temperature and activity of the reactions increase. It is then, probably, that it is formed too rapidly to be all of it fixed by the secondary reactions, and thus passes over with the distillate.

It is sometimes difficult to get a gallon of distillate below 180°, in which case the thermometer may be made to rise to 182° or 184°. A temperature of 186°, however, can never be exceeded with safety to the product, and as very little ether is formed at the close of the process, it is better to arrest it an ounce or two short of the prescribed volume, than to risk a higher temperature. If carefully managed, it is easy to control or arrest the process at any stage by diminishing or stopping off the heat; but if incautiously managed, a new and comparatively uncontrollable reaction occurs, which produces no ether, but aldehyd and hydrocyanic acid vapors in abundance. The operator should, therefore, be always in readiness to remove the receiving bottle, particularly if using larger quantities of materials than those of the officinal formula. At the end of the process the retort contains 36 f ℥ of residue in two layers. The upper one, of say 4 to 6 f ℥, is yellow, transparent and oleaginous; the lower is white or opaque from mechanical admixture of an undissolved salt. This residue should be poured at once from the retort, in order to avoid risk of losing the vessel in the attempt to get it out after it solidifies. This residue boils actively long after being poured into a cool vessel, and the vapors given off by it are hurtful.

The retort, condenser, and all the muslin, etc., used about the connections having been thoroughly washed, and the apparatus again set up, the rectification is commenced.

The carbonate of potassa having been put into the receiving bottle at the commencement of the process, and the distillate having been received upon it, the whole is now well shaken up with the palm of the hand only, over the bottle mouth, and poured into the cleansed retort, and the bottle rinsed in with the diluted alcohol. The bottle is then rinsed clean, tied over as before, and replaced in the apparatus, when the heating is cautiously resumed. At 130° to 133° the liquid will fairly boil, and must be kept from boiling too rapidly for the capacity of the condenser, as it is easy to drive off an important portion of the ether by too rapid heating at first. One-fourth of the gallon should pass over before the temperature rises above 176°, and as this portion contains nearly all the ether, the remainder being more easily condensed may be distilled more rapidly.

If the first fourth of this distillate be kept apart and distilled fractionally, it commences to boil at 68 to 72°, boils rapidly and distills fast at 74°, and then steadily and more and more slowly arises to 156°. The receiver is then changed and 8 f ℥ more distilled over. This is redistilled to 17 f ʒ. The first product measures 8 f ℥ received up to 156°, is of a golden yellow color, and has a s. g. of .8914 at 50°. The second product 17 f ʒ is of a paler yellow and has a density of .862 at 50°. The rejected portions still contain some ether, probably 3 f ʒ of the same density as the last product. By a calculation based upon the specific gravities, this would give to the officinal spirit of nitre by this process, a composition of 123 f ℥ alcohol, and 5 f ℥ of pure dry hyponitrous ether, or about 4 per cent. of the ether under the most favorable circumstances.

The sweet spirit of nitre obtained by this process is a volatile, transparent, bright liquid, of a greenish yellow tint—never colorless, and of a fragrant but not pungent odor. It boils at 156° to 158°, and has a specific gravity of .840 to .841 at 60° when freshly made. It is perfectly neutral to test paper, and gives a deep straw color with dilute solution of potassa within half an hour.

With good materials and careful manipulation this process yields an excellent medicinal preparation liable only to the objections that it contains too much aldehyd, and is not as uniform in strength, nor quite as strong as desirable. When put up at once in half pint bottles, well filled and well stopped with waxed glass stoppers, and the bottles covered with dark paper, it keeps well. Several bottles of it made in March, 1854, were examined recently in connection with this part of the subject, and were found to have undergone no perceptible change. It is the practice of this laboratory to make this preparation fresh for every vessel of large class that is fitted out in the navy, and the preparation now examined was made for the frigate Columbia, then fitted out as the flag ship of the home squadron, and was returned with the stores of that vessel when she was laid up, after a cruise of nearly two years, principally in the West Indies. As a test of the keeping properties of the preparation when well made, I regard this as conclusive. Another specimen one year and three months old, is in the same good condition.

After having practiced this process bi-monthly or oftener for two years, it was abandoned in search of a better and more convenient one, for the following reasons:

It is unnecessarily circuitous and complex.

It makes use of a salt that is often difficult to obtain free from chlorides; and that is nearly insoluble in the menstruum used, thus postponing the reactions and rendering them somewhat variable and precarious. The reaction which produces an undue proportion of aldehyd in the distillate, and which probably occurs at temperatures about 186° to 190° may very well take place in that portion of the materials confined under the cake in contact with the bottom of the retort, for it is not uncommon to see a violent boiling out from under the cake, when the ebullition elsewhere is quietly and steadily going on. There is no way of securing uniformity of temperature and reaction in a retort of boiling liquid when a cake of solid matter lies upon the bottom.

The process distills over from one-half to three-fourths of the alcohol twice unnecessarily, for the six pints first received in the etherification, and last received in the rectification, are simply alcohol. This unnecessary distillation occupies half the time of the process, and requires a larger apparatus than is commonly possessed by apothecaries.

In making nitric acid, the materials used in this process should yield practically about 18½ ℥ of an acid of 1.41 s.g., and upon this the following process is based ; and this process is the best substitute for the officinal one that I have yet tried, and its details and results are based upon an experience of nearly a year and a half :—

Take of Nitric Acid, s.g. 1.408 28 f℥ =37℥ =2 lb. 8½ oz. Av.
Alcohol, " .835 20 pints.
Carbonate of potassa, 2℥.

The apparatus required is the same precisely as that for the U. S. P. process, except that, for double the yield, both the retort and receiver may be of 2 pints less capacity. The receiver should be marked at each pint by a pencil on a slip of paper pasted vertically on the side of the bottle.

One gallon of the alcohol is introduced into the retort, the acid slowly added to it, and heat applied through the intervention of water, or preferably by a steam jet. At 178° the yellow mixture begins to boil, and faint yellow vapors appear in the retort as brisk distillation commences at 184°, the distillate being slightly yellow and ethereal from the beginning.

As the distillation proceeds, the boiling mixture and the atmosphere within the retort become more yellow till the temperature reaches 188°, and three pints have passed over. The temperature then, if watched closely, will be seen to fall from ½° to 2°, according to the amount of heat applied at the time, and coincidently with this, a material increase in the rate of distillation and color of the distillate occurs. This indicates the full establishment of the etherifying reactions, and should be carefully observed and appreciated. As soon as the distillation increases and the temperature begins to fall, the heat should be moderated down, and as soon as the reaction is fully established, the heat should be entirely withdrawn. The thermometer then falls very slowly and steadily to 170°, the distillation also decreasing till at 170° about 5¼ pints of distillate have passed over. The heating is then cautiously resumed, and the thermometer kept steadily at or about 176° till 6½ pints have passed over, when the process is terminated and the apparatus taken down, thoroughly rinsed out, and set up again.

The carbonate of potassa is added to the distillate and well shaken with it, the bottle being closed only with the hand. The mixture is then poured into the retort, and the rectification commenced, slowly at first, or at least with a speed proportionate to the capacity of the condenser. The mixture boils at about 80°, distills rapidly at 100°, and 18 f℥ should pass over before the temperature rises above 150°. The heat may then be increased from time to time, and the remainder pushed over rapidly till 5½ pints have been received. The distillate is then transferred to a larger vessel, alcohol added to it till it measures 17 pints, the whole well shaken, and then put up in half pint bottles, well filled, and well stopped with waxed glass stoppers, and the bottles covered with dark blue paper. The whole process occupies about 4 hours.

The product is neutral, of a clear bright yellow tint, and fragrant odor, free from pungency. The s. g. is .841 to .842, it boils at 156° to 157°, and gives but a pale straw color with dilute solution of potassa within half an hour. It is occasionally so free from aldehyd that several hours is required to develop the color with solution of potassa. The tint is generally seen within an hour by looking through the test tube in the directien of its long axis. The comparative freedom from aldehyd, for it is never altogether free from it, is an indication of the care and success with which the process has been conducted, and is, too, an indication of the length of time the preparation will keep in dispensing. Put up as above directed, this preparation has kept for one year without the slightest appreciable change. How much longer it will keep, I am not able to say at present.

If, in the rectification of the above product, the distillation be conducted fractionally and the different portions of the distillate examined, they will be found nearly as follows:—

18 f ℥	received	up to	150°	golden yellow,	s.g. .900	at 50°
2¼ f ℥	“	“	160°	pale straw,	“ .878	“ 57°
6½ f ℥	“	at	160°	paler “	“ .869	“ 56°
10 f ℥	“	up to	176°	“	“	not examined.

The last portion, not examined, probably contains 1¼ f ℥ of ether, of s.g. .869, at least, in which case a calculation by the specific gravities indicates that this preparation contains very nearly 14 f ℥ of dry hyponitrous ether, s.g. .947, or about 5.1 per cent.

In adopting the proportions of this formula I supposed it would yield a preparation medicinally identical with that of the U. S. P. process, and this supposition, based upon a practical observation in making nitric acid, was strengthened by the physical properties of the resulting spirit of nitre. I have since found, however, as now stated, that the 18½ ℥ of nitric acid of s.g. 1.408 that the United States Pharmacopœia materials do yield when distilled separately is not utilized in that process, for if the ready-made acid in this quantity is substituted for the materials for generating it, the yield of ether is over 1 per cent. more in the preparation. The U. S .P. process should yield a preparation containing 5 per cent. of dry ether, but cannot be made to do so in my hands except by obtaining the nitric acid as a separate operation. Why the acid yields one-fourth more ether than I can obtain in using the materials for generating it, I could only attempt to explain upon theoretical grounds, which I do not fully entertain in opposition to the practical experience upon which the Pharmacopœia process is based.

This process of obtaining a dilute hyponitrous ether, and then farther diluting it, is quite applicable to general pharmaceutical use, and from the experiments I have made for reducing the scale with this view, I venture to assert that any apothecary who can compound a prescription properly can as easily make this preparation for himself. It is one of those preparations, and the number of such is not few, that is more easily made upon the small scale, simply because the success that attends the process depends mainly upon a temperature, and because this is more easily regulated in small vessels with small quantities of materials to react. It can be made very cheaply too, and with an apparatus so simple, and of so general an adaptability, that a great majority of apothecaries doubtless always possess it.

Having recently bought such an apparatus for making these experiments on the small scale it may be worth while to enumerate it, and mention the cost.

A tubulated retort 14 to 16 f ℥ capacity.......cost	$0	42
A tubular thermometer* .... "	1	75
A piece of thin glass tube, ½ inch internal diameter and three feet long; and two short pieces of small glass tube which may be bent in the lamp ....cost		13
And two feet of small India rubber tubing .... "		25
	$2	55

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* These thermometers are imported from Germany. They are by far the most convenient and useful. They consist of an opaque glass scale and capillary tube with black figures, enclosed in a glass tube not much larger than that of a barometer. Being entirely of glass, except the enclosed mercury, they are well adapted to an extended and indiscriminate use.

They may be had of J. F. Luhme & Co., No. 565 Broadway, or of F. Liese, No. 102 John Street, New York, of Mr. A. P. Sharp, of Baltimore, and probably also of apparatus dealers generally.

Of these last materials I made a very good Liebig's condenser with corks, by soldering together two plaster cans for a case. The necessary lamp and stand, vessel for a water-bath, and proper supports, are always at hand in some form that may be made available. With such appliances the dispensing apothecary can, and should make this preparation for a length of time proportionate to the care and skill with which he uses them, with great advantage to himself, to the patient and to the physician.

Take of Nitric Acid,	s.g. 1.408	2 f℥.
(or " "	" 1.35	2½ f℥)
Alcohol,	" .835	22½ f℥)
(or "	" .838	21 f℥)
Carbonate of Potassa,		2ʒ.

The apparatus being set up, add the nitric acid slowly to 9 f℥ of the alcohol in the retort, and having the thermometer in place, apply the heat. The mixing of the materials gives them a temperature of 93° to commence with. If the nitric acid used is nearly colorless the mixture will be colorless also till heated to near the boiling point, when it becomes yellow.

It begins to boil at 179° to 181° and boils and distills actively at 184°, yielding a yellow distillate from the first. It occasionally happens that this, in common with many other liquids, boils badly, becoming heated far above the boiling point, and only boiling at intervals and by bursts of ebullition. This curious condition of fluids commonly occurs in small round bottomed glass vessels, and may be measurably controlled by having a fragment or two of glass in the retort. These should not be dropped in while the liquid is heated above its boiling point, as they then almost invariably cause it to boil over, but the process should always commence with this simple precaution.

The mixture goes on boiling and distilling steadily at a temperature gradually and slowly rising to 186° or 187° where it becomes stationary till 7 f℥ of distillate has passed over. The heat is then moderated by lowering the lamp till the temperature falls to 176°, and the distillation continued about this point till the distillate amounts to 8 f℥, when the first part of the process is terminated.

During this distillation the temperature is liable to fall suddenly a degree or more, and then slowly rise again. Such variations of temperature may be disregarded as long as the rate of distillation continues unchanged; but if coincidently with a fall of temperature the distillation should increase and gases pass over uncondensed, the lamp should be at once removed. The temperature will then continue to fall steadily to 170° while the distillation slackens, when the heating may be cautiously resumed till the prescribed 8 f ℥ has been received below 176°.

The apparatus is then thoroughly rinsed out, the distillate returned to the retort, the carbonate of potassa added to it, the whole shaken round well without splashing into the retort neck, the apparatus connected, and the warm water of the bath carefully and slowly applied so that the distillation does not exceed the capacity of the condenser. This capacity is easily and nicely determined by watching the drop which always occupies the end of the small eduction tube fitted to the end of the condenser. If the condenser is working below its capacity, bubbles of air will from time to time pass *into* the apparatus, and the delivery will be irregular from this tendency of air to pass in, by or through the condensed liquid. If working beyond its capacity the drops will be blown out by escaping vapors. The first part of the rectification should not proceed too slowly, however, for the distillate then, from being nearly pure ether, evaporates rapidly, particularly if received in a large mouthed vessel.

As a guide to the strength of the preparation, it is proper to notice that about 1 f ℥ should pass over before the temperature of the boiling liquid rises above 150°, and that by the time the temperature reaches 176°, 3 f ℥ should have been received. This 3 f ℥ of distillate should have a s.g. of .869.

The rectification is carried to 6 f ℥, and this distillate is diluted to 19½ f ℥ with the remainder of the alcohol, and well shaken. It should then be transferred at once to small bottles well filled and stopped, and covered with dark wrappers.

If the first distillate be rectified fractionally, it will yield as follows :

1 f ℥	up to	157°	golden yellow	s.g.	.8944	at	54°
1 f ℥	"	173°	paler	" "	.8640	"	60°
1 f ℥	"	176°	paler	" "	.8483	"	60°

giving a mean s.g. for the first 3 f ℥ of .869. The remaining 3 f ℥ is nearly colorless, and almost wholly alcohol.

Assuming that the first 3 f ℥ is a solution of hyponitrous ether in alcohol, it will consist of 7.94 f ʒ of the ether and 16.03 f ʒ of alcohol, and will therefore yield a finished preparation containing 5.1 per cent. of dry hyponitrous ether.

I have found in practice that nitric acid which is sold as "1.42" s.g. commonly has a true s.g. of 1.405 to 1.41, and the commercial acid sold as "1.38" is often as low as 1.35 in reality. So alcohol sold as ".835" is rarely below .836 and often above .838, whilst I have not yet seen a specimen of "95 per cent." alcohol that was in reality below .8195 to .820 s.g.

If the second set of proportions given in brackets in the formula be used with these commercial materials that are not weaker than the specific gravities given indicate, the mixture will boil at 180°, but the boiling point will not rise so high as 186° till near the end of the distillation. Then, however, it is prone to rise higher and to produce more aldehyd in the distillate if not very carefully and slowly conducted. The same quantity 8 f℥ should be distilled over, and at similar temperatures. In the rectification about 7 fʒ will pass over below 150° to 156°, and 3 f℥ below 176°. The rectification should be carried to 5 f℥ only, and to this should be added 11 f℥ of alcohol, making 1 pint of finished sweet spirits of nitre.

The s.g. of the 20 fʒ first received in the rectification is .8732 which yields by calculation 6.94 fʒ of the ether s.g. .947, and 13.06 fʒ of alcohol s.g. .838, thus furnishing a product containing 5.2 per cent. of the dry ether, or practically the same with the other materials.

This preparation cannot be distinguished from the other by appearance or sensible properties, is neutral to test paper, but has a very different s.g.—.847 instead of .8415—and is liable to contain more aldehyd. Of its keeping properties I can say nothing, only that I believe that sweet spirit of nitre keeps best when it contains least water; and that much water will cause it to spoil very soon, no matter how carefully it may be kept.

Except that ordinary nitric acid is almost as liable to contain chlorine, as nitrate of potassa is to contain chlorides, the first of these processes on the small scale is nearly unobjectionable in practice, chiefly because the proportions of acid and alcohol are such that etherification occurs near the boiling point of the mixture, and near the boiling point of alcohol, where the temperature is most easily regulated. It avoids the violent reaction and difficult management of the Edinburgh and Dublin processes, and also avoids the loss attending the separation and manipulation of so volatile a liquid as these processes obtain, for as the alcohol distills over with the ether, and as the ether is slowly produced, its volatilization or loss is measurably controlled.

When the alcohol bears a smaller proportion to the acid than that given, the boiling point of the mixture is higher, and the reactions occurring at a higher temperature produce more aldehyd in the distillate, and are less easily and less economically controlled. When a much larger proportion of alcohol is used, it distills off before the proper reactions take place, the distillation of unchanged alcohol frequently continuing till the proportion is considerably less than that adopted in the formula, and the reaction when it does occur is of course correspondingly more active. The manner in which nitric acid and alcohol are mixed has a most interesting and important bearing upon the character of the reactions, as well as upon the period and rate at which these reactions occur. Thus the acid, if new and colorless, may be so slowly and carefully mixed with the alcohol that in the proportions given in the London officinal formula the whole of the prescribed distillate may be drawn over before any appreciable reaction occurs. In practice, upon a scale of 2½ gallons of materials, this has twice occurred to me, without any particular care, or premeditated slowness in mixing. On the other hand, if alcohol is slowly poured into nitric acid, a most violent reaction occurs before the proportions become equal, and this violent reaction continues long after the proportions pass the limit of 5 to 1, or until the cold alcohol quenches the reaction altogether. Such a mixture has the sensible properties of spirit of nitre. At some period, and in some portions of all mixtures as ordinarily made, some of these conditions of concentration are liable to occur, and thence to act as a starting point from whence general reaction may commence earlier or later, as the case may be. Hence the utility of a proper proportion, and of a temperature regulated at the lowest point of equable reaction, as the best, the safest, and the most economical means of controlling such variations in the reactions. The means of controlling within narrow practical limits, the strength of the preparation by the proposed formula is very satisfactory, and not difficult to accomplish. It consists simply in taking the specific gravity of that portion of the distillate in the rectification which comes over below the boiling point of alcohol, which portion will contain nearly all the ether, and may for practical purposes be considered as a solution of hyponitrous ether in a small proportion of alcohol. The operator will then have three specific gravities; namely, of the mixture and its two elements (the small portion of water and aldehyd, and degrees of temperature within five or six being disregarded), from which to calculate the proportion of each element, by the following rule:

"Take the difference of every pair of the three specific gravities; viz., of the compound and each ingredient; and multiply the difference of every two by the third. Then as the greatest product is to the whole weight" or volume "of the compound, so is each of the other products to the weight" or volume "of the two ingredients." The specific gravity of the mixture being above or below the mean of the two ingredients, indicates that the largest obtained proportional belongs on the side of the greater or less specific gravity.

The descriptions of sweet spirit of nitre as commonly met with are faulty. It is described by our Pharmacopœia in common with others as "colorless." I have never seen it colorless when of fair quality, no matter by what process it may have been made. On the other hand, when of full officinal (U. S. P.) strength, it has a very decided greenish yellow tint. That it may be made colorless by repeated rectification of the ether, I have no doubt; neither of the formulas, however, accomplish this. It is said that it "slightly reddens litmus," but when freshly made, or when well kept, it does not at all redden ordinary litmus paper until a few moments' exposure to the air, on the paper, oxidizes the aldehyd or binoxide of nitrogen which it contains, in small proportion. This change occurs the more quickly, and is the more marked, as the preparation contains more water. The strictly officinal preparation begins to boil at 156° to 157° instead of "160°." It is described as having a s.g. of .834, a density below that of the alcohol used, whilst the ether dissolved in the alcohol has a density of .947. In practice the s.g. varies from .840 to .841 when freshly made. It, however, loses in s.g. and in color, by age, without giving evidence of any other change. Several specimens put up at .840 to .842 were examined at periods varying between two years and five months, were found to have s.g. of .835 to .838 yet were not deficient in the proportion of ether yielded to fractional distillation.

Tests of character for this preparation are much needed, but it is not easy to find any that are simple and reliable. The least objectionable method of estimating or comparing the ethereal strength is probably that of fractional distillation. One pint of officinal sweet spirit of nitre distilled from fragments of glass, by a water-bath, yields a yellow distillate of one-fourth of its bulk, whilst the temperature in the boiling liquid is below 180°, and such a distillate contains nearly all the hyponitrous ether of the preparation. This distillate, again distilled in precisely the same way, yields 1 f ℥ of distillate below 176°. This last, upon the addition of an equal bulk of water, added in a stream, and without agitation, yields a supernatant ethereal layer of 2½ f ʒ. The preparation by the proposed process yields about 3 f ʒ. These results are based upon a number of trials, and are not too high, but will be found to indicate the comparative value very conveniently. Dilute solution of potassa, say equal parts of officinal solution and distilled water, is an excellent test for aldehyd in a spirit that is free from acid or nearly so, provided time be given for its reaction to develop the color. I have never seen a specimen of good spirit of nitre that would not, in the proportion of equal parts, yield a decided straw yellow tint with this test within twelve hours. A yellow tint is usually perceptible within fifteen minutes, and the color thence grows deeper for twelve hours, when it becomes of a golden or brownish yellow of a deep hue. Where aldehyd is in undue proportion, this change occurs sooner, and becomes ultimately of a brown hue, even within an hour or two. The changes appear to take place more quickly in warm weather, and in a bright light.

The sulphuric acid test is less convenient and less to be relied upon in my hands.

In order to ascertain the relative strength the officinal preparation bears to the commercial article as supplied to apothecaries generally, six samples of sweet spirit of nitre were purchased and examined. Five of these samples were obtained from five of the largest and most respectable wholesale drug establishments in New York city, and one from a large establishment that is considered to be of second rate as to character. As these houses represent the commerce in medicines, under the most favorable circumstances, so the samples obtained from them may be considered as fairly representing the merchantable articles and the manufacturers that supply the demand. The six samples were sold as the products of three manufactories, two of Philadelphia, and one of New York. Two of these manufactories are very extensive, and probably supply a very large proportion of the medicinal preparations that are manufactured in the United States. The third is much smaller, and represents a pretty numerous class of manufacturers of special preparations. Three of the samples are alleged to be from the largest manufacturers, two from the second in extent, and one from the smaller. One of these manufacturers makes and sells five different kinds of Sweet Spirit of

Nitre. Only two of these were examined, however, as these only, called "3 F" and "4 F" were met with in casually purchasing the six samples as a fair representation of the article that is now within the reach of general medical practice.

These specimens, then, probably represent the manufacture and the markets of New York and Philadelphia in this preparation. They were carefully examined by fractional distillation as above mentioned, and are placed in comparison with No. 7, which is a strictly officinal U. S. P. preparation 16 months old.

No.	Color.	S.G.	Reaction with Litmus.	Reaction with Sol. Potassa in 15 minutes.	Ethereal layer separated by water from 1 pint of spirit	Estimated percentage of dry Ether contained.	
1	Good.	.839	Neutral.	Yellow.	50 ♏.	Below 1.7 p.c.	
2	Pale.	.840	"	"	1 f ʒ scant.	" 2. "	
3	Good.	.839	"	"	1 f ʒ	" 2. "	
4	Good.	.881	Acid.	Colorless.	1 f ʒ scant.	" 2. "	"4F."
5*	Colorless.	.911	"	Brown.	None.	" 1. "	"3F."
6	Good.	.851	Slightly acid	Yellow.	1 f ʒ 35 ♏	3.16 "	
7	Good.	.840	Neutral.	"	2¼ f ʒ	4.2 "	

It would appear from this table that a great majority of the physicians, whose patients obtain their Sweet Spirit of Nitre from ordinary sources, are prescribing a preparation that is considerably below half its proper strength; or often but little more than dilute alcohol. It is not surprising that little or no medicinal effect is obtained from such an article; or that when given in the now common doubled dose it produces the almost opposite effect of so much alcohol.

The officinal U. S. P. preparation is at best probably too strong in alcohol for the full medicinal effect of the hyponitrous ether, having probably less ether in it by 1 per cent. than the framers of the Pharmacopœia purposed it should have from the formula.

Hence the physician who predicates any part of the character of his profession upon the diaphoretic, diuretic, or febrifuge effects of this commercial preparation too often brings a discredit upon his science and art, which more justly belongs to the preparation he employs. His patient distrusts his skill, and instinctively seeks for better results from some of the various pretended "systems" or quackeries with which he is surrounded.

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* This sample was opalescent when purchased, and this "muddiness" was ascribed by the person who dispensed it, to his having "rinsed out the bottle with water" previous to putting it up. In standing twenty-four hours it became clear by depositing a white sediment.

It is not probable that bad colocynth or bad scammony are ever to be found in "Brandreth's Pills," but I have good reason to believe that the seed from the colocynth of which Brandreth's Pills are made, is separately powdered and sold, and that from such cheap varieties of powdered colocynth much of the extract is made upon which regular practitioners must rely.

In view of such illustrations, is it surprising that charlatanism flourishes, or that medical men are to be found in co-partnership, or in competition with it? The patient often doubts the quality of his physician or of his physician's science, but rarely reflects upon the tendency of commercial competition and a blunted moral perception upon the means on which physicians must rely.

It is said of Sweet Spirit of Nitre, as of Hoffman's anodyne and other preparations, that the commercial article is so very different from that contemplated in the materia medica, that it may be well to examine into the expediency of so modifying the Pharmacopœia as to produce the commercial article, because the curative effects or character of the article as a remedial agent must belong to it as found in commerce, rather than as produced by the officinal formula, since by far the greater part used in medicine is obtained through commerce. To all such reasoning and expediency, and to the increasing disposition to subsidize every science and art to the making of money alone, I offer my hearty and unqualified opposition; for it is mainly thus that the physician is losing one by one his valuable curative agents, and acquiring for his profession an uncertainty which does not belong to it, but which engenders a popular distrust as injurious to that profession as it is beneficial to charlatanism.

U. S. Naval Laboratory, New York, May, 1856.

At the revision of the U. S. P. of 1860, the writer, serving in that revision, offered the amended process above given. This, after full discussion and repeated trials by other members of the Committee of Revision, was slightly changed and adopted, the name of the preparation being also changed to that since used.

Ten years' work with this process in the writer's hands suggested a few improvements in the details, but the plan of direct distillation of nitric acid and alcohol alone, was always used, and no important criticism of the U. S. P. process was offered. Yet, in the revision of 1870, the Committee of Revision changed the process very much. The British Pharmacopœia had been revised and published in 1867, and a process arranged by Prof. Redwood had been there adopted, wherein metallic copper and sulphuric acid were added to the reaction between the nitric acid and alcohol on theoretical grounds. The reasons given for this change were at first accepted by the writer, and the process was very thoroughly tried, but without the promised advantages,—without any advantage,—and the process was soon abandoned for the former one. The Committee of Revision of 1870, however, adopted this process, copying the British Pharmacopœia very closely in everything excepting in the strength and quantity, or proportion, of alcohol used. The other elements being kept the same, the alcohol was increased by nearly one-half, thus reducing the strength of the product to nearly one-half that of the British Pharmacopœia, and to less than one-third the strength of the U. S. P. of 1860. As no notice was taken of this great change in strength by the Pharmacopœia, nor any explanation ever offered, it has always been supposed by the writer to have been unintentional. But if ever discovered by the Committee it was never corrected, and continued to be the officinal practice for the entire ten years. The supposition that it was an unintentional change is strengthened by the circumstance that the description and tests were kept practically the same for this as in 1860 for a preparation more than three times stronger.

And the supposition that the mistake was not discovered by the Committee is strengthened by the circumstance that the Committee of Revision of 1880 failed to correct it, although they gave a product somewhat stronger,—or, of nearly half the strength of that of 1860.

The Committee of 1880 revised the process materially by leaving out the copper of the British Pharmacopœia, but retaining the sulphuric acid;—by washing the crude ether;—and by reducing the amount of the alcohol of dilution. Yet still this Committee practically adhered to the description and tests of 1860.

The revision of 1860 followed this writer in stating that the product contains from four and three-tenths to five per cent. of its peculiar ether (not necessarily ethyl nitrite). The revision of 1870 reduced the strength to less than one-third, and yet states that it contains 5 per cent. of its peculiar ether. The revision of 1880 yields a product of less than half the strength of that of 1860, and yet claims that it contains at least 4 per cent. of real ethyl nitrite.

Whenever nitric acid of anywhere near the pharmacopœial strength is distilled to the end of the reaction with alcohol that is also near to the pharmacopœial strength, the product is a complex ethereal liquid which is fairly uniform in quantity and quality, and the amount produced is in direct proportion to the nitric acid used. This complex ethereal liquid contains a fairly uniform proportion of ethyl nitrite, and when it is diluted with alcohol, to a definite degree, it forms spirit of nitrous ether.

The stochiometric proportions for reaction between nitric acid of s.g. 1.42 at 15.6° C. (compared with water at the same temperature) and alcohol of s.g. .814 at 15.6° C. are about 13 parts acid to 14.2 parts alcohol, but unless the alcohol be taken in larger proportion, the reaction is so active as to involve serious loss. But if the proportion of alcohol be very much increased the reaction does not occur until the excess is distilled off. And again, as the acid becomes reduced and diluted toward the end of the reaction, the excess of alcohol comes over partially or entirely undecomposed. Within fairly uniform limits, however, and under the pharmacopœial conditions, the relation between the quantity of nitric acid taken, and the quantity of the finished spirit of nitrous ether, indicates the strength of the spirit. Therefore the confusion into which the subject seems to have drifted is shown by this relation.

The first U. S. P. of 1820 started this preparation aright by the direct distillation of nitric acid and alcohol in such proportion as to yield from 4.5 to 5 p.c. of the ethereal liquid in the product, and the relation of the nitric acid taken, to the finished spirit of nitrous ether, was about 1 to 4.8.

The first revision of the U. S. P. in 1830 changed from nitric acid to potassium nitrate and sulphuric acid, using such proportions as to keep the nitric acid about the same, and the relation of the nitric acid given by the potassium nitrate, to the finished spirit of nitrous ether, was about 1 to 4.6.

The revisions of 1840 and 1850 adhered to this formula of 1830. Before the revision of 1860 the writer showed in the paper reproduced here, the objections to this process;—showed that it did not yield the strength of product required by the calculated amount of nitric acid, but gave a relation of 1 to 5.5 instead of 1 to 4.6;—and showed that it was desirable to get back to the process of 1820, but that the 1 to 5.5 strength having then been established by 25 years' usage, had better remain practically unchanged. These efforts in the Committee of 1860 were successful, and the practice of the direct distillation of the elements was resumed and the relation of strength of about 1 to 5.5 was preserved; and, throughout the 50 years from 1820 to 1870 the proportion of ethereal liquid in the finished spirit was from 4.5 to 5 p.c., and the proportion of ethyl nitrite must have been about 4 p.c.

In 1870, however, the very radical change was made of following the British Pharmacopœia in all points excepting the proportion of alcohol. The British relation of strength was about 1 to 10.7 of finished spirit. But the U. S. P. of 1870 was about 1 to 19, or less than one-third the strength of the past 50 years.

At the time this change was made the writer did not suspect its radical character, and rather carelessly endeavored to adopt its proportions. But having occasion to send a sample from his stock to Mr. A. H. Allen, possibly at Mr. Allen's request, it was reported by Mr. Allen to be very deficient in strength, whereupon the writer at once went back to the old process of 1860.

In 1880 the process was again materially changed and the relation of strength became about 1 to 13 of finished product. The German Pharmacopœia is about 1 to 7.7.

The object of this paper is once more to try to get the Committee of Revision of 1890 to return to the strength of 1860; or else let the medical profession know that its spirit of nitrous ether is so weak as to approach the commerical article of the markets in uselessness.

ETHYL NITRITE.

A very valuable paper on "The Preparation of Ethyl Nitrite," by Professor Dunstan and T. S. Dymond, of the Research Laboratory of the British Pharmaceutical Society, is published in the *Pharmaceutical Journal and Transactions*, of April 14, 1888, p. 861. By a slight modification of the process given in this paper on ethyl nitrite supposed to be pure, was twice made. The s.g. of this liquid compared with an equal volume of water at the same temperature, was .9177 at 4°C. The boiling point was so low that the s.g. could not be taken at 15.6°C., but when mixed in equal weights with nearly absolute alcohol of the s.g. .8033 at 4°C., or .7943 at 15.6°C., the s.g. of the mixture was .8579 at 4°C., or .8447 at 15.6°C. The mean of the two specific gravities at 4°C. in the mixture being (.9177+.8033=1.7210÷2=) .8605, and the observed s.g. .8579 appears to show an expansion of .0026 at 4°C. The s.g.

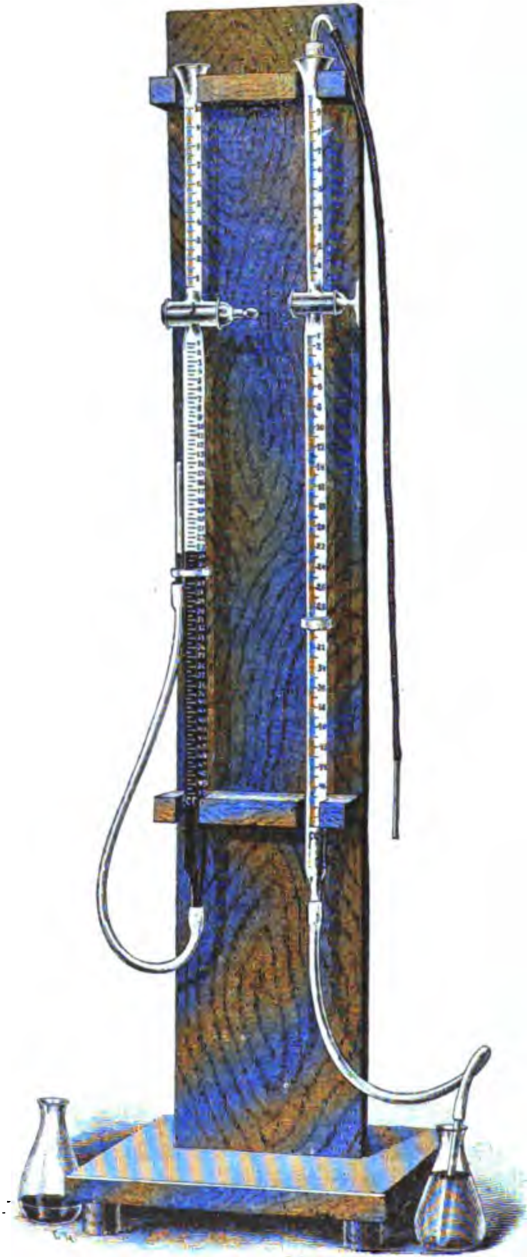
of this ethyl nitrite at 15.6°C., as deduced from these data, would be about .8977.

This ethyl nitrite was then used for making the dilutions now to be mentioned.

All the dilutions contained 5 p.c. of this ether; and the weighings were as close as was easily practicable with liquids so volatile, and were made at common room temperatures. The specific gravities given are comparisons with water, at the same temperatures, as the unity standards, and these were taken in the 100 gram. s.g. bottles shown at p. 1166. The 5 p.c. solutions were all assayed for the proportion of ethyl nitrite by the method of Mr. A. H. Allen, of Sheffield, England (see his "Commerical Organic Analysis," 1885, vol. I., p. 150, and valuable papers in The Pharm. Jour. and Trans. for Feb. 21, 1885, p. 673, and Nov. 21, 1885, p. 440.) A slight modification of Lunge's Nitrometer, as figured in Sutton's Volumetric Analysis, 5th edition, p. 479, was used, and as it proved so convenient in use it may be worth while to show it by an illustration on the following page, 1196. The principle is, however, exactly that of Mr. Allen.

THE NITROMETER.

These nitrometers are most conveniently used in pairs, and upon a stand as shown;—or on the backboard of the stand, without the foot, screwed or hung against some wall or partition at a height convenient for filling and reading. The brine used for charging is a filtered, saturated solution of common salt, to which about 5 p.c. of water is added to avoid the separation of crystals at the line of contact with the spirit. In the illustration one nitrometer is shown in readiness to be charged with the brine from the full flask, by mouth suction, through the tube temporarily connected at the top by a cork and small suction tube. The brine being drawn up a little above the stopcock, that is closed, the cork and suction tube are removed, and the brine above the stopcock is cautiously let down into the lower tube. Then the 3 c.c. of spirit of nitrous ether is measured in a narrow pipette, which delivers the 3 c.c. with known accuracy, at the bottom of the upper graduated tube of the nitrometer; and it must be remembered that any error in quantity here is multiplied many times in the result. The spirit is then let in slowly on top of the brine. Then, 5 c.c. of a solution of potassium iodide of the strength of 2 grams. in 5 c.c. is measured into the



PHOTOELECTROTYPE ENG. CO. N.Y.

MODIFIED FORM OF LUNGE'S NITROMETER.

upper graduated tube of the nitrometer, and let into the spirit. This addition always liberates a proportion of gas which is very variable,—rarely twice alike even from similar materials and apparent conditions. This liberation of gas has been said to be due to acidity in the spirit, but it occurs with spirit that is entirely neutral or even alkaline. It is true that enough ammonia may be added to any spirit to prevent it, and this also prevents the liberation of free iodine by converting the iodine into ammonium iodide. But the gas liberated from a spirit that is quite neutral to neutral litmus paper will often liberate gas to the amount of 6 or 8 c.c., and occasionally as much as 10 or 12 c.c. This reaction is not satisfactorily accounted for, but it is not a trustworthy indication of the acidity of the spirit tested. In a very strong, freshly made spirit the addition of a similar volume of water will cause the liberation of nearly as much gas. Finally, 5 c.c. of a dilute sulphuric acid,—2 grams. in 6,– is passed in slowly, only half a c.c. or so at first. When the vigorous part of the reaction is over, the brine flask, with the end of the tube still immersed, is raised nearly to a level with the liquid in the nitrometer, and the tube is taken out and slipped through a rubber ring on the nitrometer, as shown in the one on the left of the illustration, the liquid in the two tubes being brought to the same level. The heat generated by the reaction in both the gas and the liquid prevents a correct reading at first, and, therefore, the apparatus must be allowed to stand, with an occasional readjustment of the levels until the levels no longer need readjusting. This requires some 10 or 15 minutes' waiting, and during this time the other nitrometer of the pair may be used. The final reading is then made, and the nitrometer is washed out ready for another observation while waiting for the second one to cool. By the use of the very strong iodide solution and acid, the excess is so great as to insure a fairly complete reaction without agitating the nitrometer. Yet it may easily be agitated if desired, or if very accurate results are aimed at, but the increase of gas, on waiting 10 or 15 minutes after agitation, is rarely more than .3 c.c., and this is quite within the sphere of unavoidable errors of the process. With very weak spirit the reaction is correspondingly slow, and the waiting time must be longer, or until bubbles of gas nearly cease to rise in the liquid. When a spirit containing less than 3 p.c. is to be tested, the errors are reduced by using 5 c.c. instead of 3. But if 5 c.c. of a 5 p.c. spirit be taken, the gas will extend below the 50 c.c. graduation of the nitrometer.

If nitrometer observations are made at temperatures which vary more than two or three degrees, and such observations are to be compared, it is well to make a rough correction for the difference, since the amount of gas varies $\frac{1}{273}$ of its volume for each 1°C. Such a correction is easily made by mutiplying .0037 by the number of c.c. of liberated gas, and then multiplying that product by the number of centigrade degrees for which the correction is to be made. The result is to be added to the volume of the gas when the temperature to be corrected is below the common room temperature, or is to be subtracted from the reading if above. Thus .0037 multiplied by 31.5 c.c. of gas gives .11655, and this multiplied by 2.5°C. difference of temperature between two observations which are to be compared, gives .29+c.c. to be added to the 31.5 c.c. of gas if that was below, or be subtracted if above the temperature of the observation with which it was to be compared, giving (31.5+.29=) 31.79 in the one case, or (31.5—.29=) 31.21 in the other. Such a correction makes a difference in the result of about .09 p.c. of the nitrite.

In order to get a standard for the nitrometer work, a solution of pure ethyl nitrite, made by the process described by Prof. Dunstan and Dymond, was accurately made, in the proportion of 5 p.c. by weight, in nearly absolute alcohol (99.84 p.c.), and this solution, having a s.g. of .7995 at 15.6°C., was carefully and repeatedly tested by the nitrometer. The resulting indications, at room-temperature of about 20°C. or 68°F., were, for 3 c.c. of the 5 p.c. solution (=.7995×3=2.3985 grams.) on an average, 33.33 c.c. of liberated gas. This gives (33.33÷3=) 11.11 c.c. of gas for each c.c. of a 5 p.c. solution of ethyl nitrite, and therefore 33.33÷5 p.c.=) 6.66+c.c. of liberated gas from 3 c.c. of solution, indicates 1 p.c. of ethyl nitrite; and it follows that the number of c.c. of gas liberated from 3 c.c. of any spirit of nitrous ether, divided by 6.66, will give the percentage of ethyl nitrite,— or of the nitrites,—which it may contain, and this is adopted as the standard for the measurements.

The use of the nitrometer, as here indicated, is not regarded by the writer as being entirely trustworthy,—not simply because corrections for temperature and barometric pressure are omitted,—but because of conditions of slight variability in its indications which have not been investigated. But its use in a process of assay for spirit of nitrous ether is so much easier than the apparatus and process of Eykman, and so much better than any other that has been proposed, that its errors and imperfections are far overbalanced by its practical utility, and the great need for some such instrument. A difficulty in the way of its general application is that it is not accessible to all who need it most, and an effort to substitute for it a simple device which can be made by anyone, will be described farther on. Nitrometers are very well made by Mr. Emil Greiner of No. 63 Maiden Lane, New York, N. Y., at a cost of about $3.00 each or $7.50 for a pair with a stand, as in the illustration.

In the use of the nitrometer by Mr. A. H. Allen's method of testing spirit of nitrous ether a few trials were made to compare the results from the use of mercury, instead of brine as recommended by Mr. Allen. But it was found that mercury could not be used with as much accuracy as brine, because of the difference in s.g. of the column of liquid above the mercury, and the consequent variability of height in the column of mercury required to balance this liquid.

In testing the effects of dilution upon the indications of the nitrometer, an observation of much significance in regard to the decomposition of spirit of nitrous ether was repeatedly made. When 3 c.c. of a strong, freshly made neutral spirit of nitrous ether was let in on top of the brine in each of two nitrometers, and was followed in one by 5 c.c. of distilled water, and in the other by 5 c.c. of the potassium iodide solution, gas was liberated from both.

From the portion	diluted with water	with iodide solution.
The gas liberated in about 1 minute measured	8 c.c.	2 c.c.
The gas liberated in about 15 minutes measured...	14.4 "	4.8 "
The gas liberated in about 12 hours measured.....	18.8 "	22.0 "
When the iodide solution was added to the first the volume of gas liberated increased to...........	26.5 c.c.	
Finally, when the 5 c.c. of acid was added to each, the volume of gas increased to.............	40.6c.c.=6.15 p.c	38.8 c.c=5.88 p.c.

The same spirit, tested by the same nitrometers, in the usual way,—that is, by waiting 15 or 20 minutes for temperature adjustment before the final reading,—gave 42.2 c.c. of liberated gas, equal to 6.4 p.c. nitrites, in each of the two, the room temperature being 22 to 25°C. throughout the two pairs of testings. The discrepancies, until better accounted for, must be charged against the process. But the effect of water in decomposing the nitrites in spirit of nitrous ether is unmistakable, and the results justify the writer's contention for many years past, that the strongest alcohol should alone be used for this preparation. A number of trials showed conclusively that the stronger the spirit was, the more gas was liberated from it on dilution with water,—and that the effect of dilution with water on the spirit of nitrous ether is greater than upon alcoholic solution of pure ethyl nitrite.

EXTEMPORANEOUS NITROMETER,

OR RUDE SUBSTITUTE FOR LUNGE'S NITROMETER.

Physicians and pharmacists are those who most need to know the character of the spirit of nitrous ether they use, yet very few of them have nitrometers, or are within easy reach of those who have, and hence it is important to find, if possible, some simple form of apparatus by which the principle of the nitrometer may be applied by any one, so as to extend the utility of the principle among those who need it most.

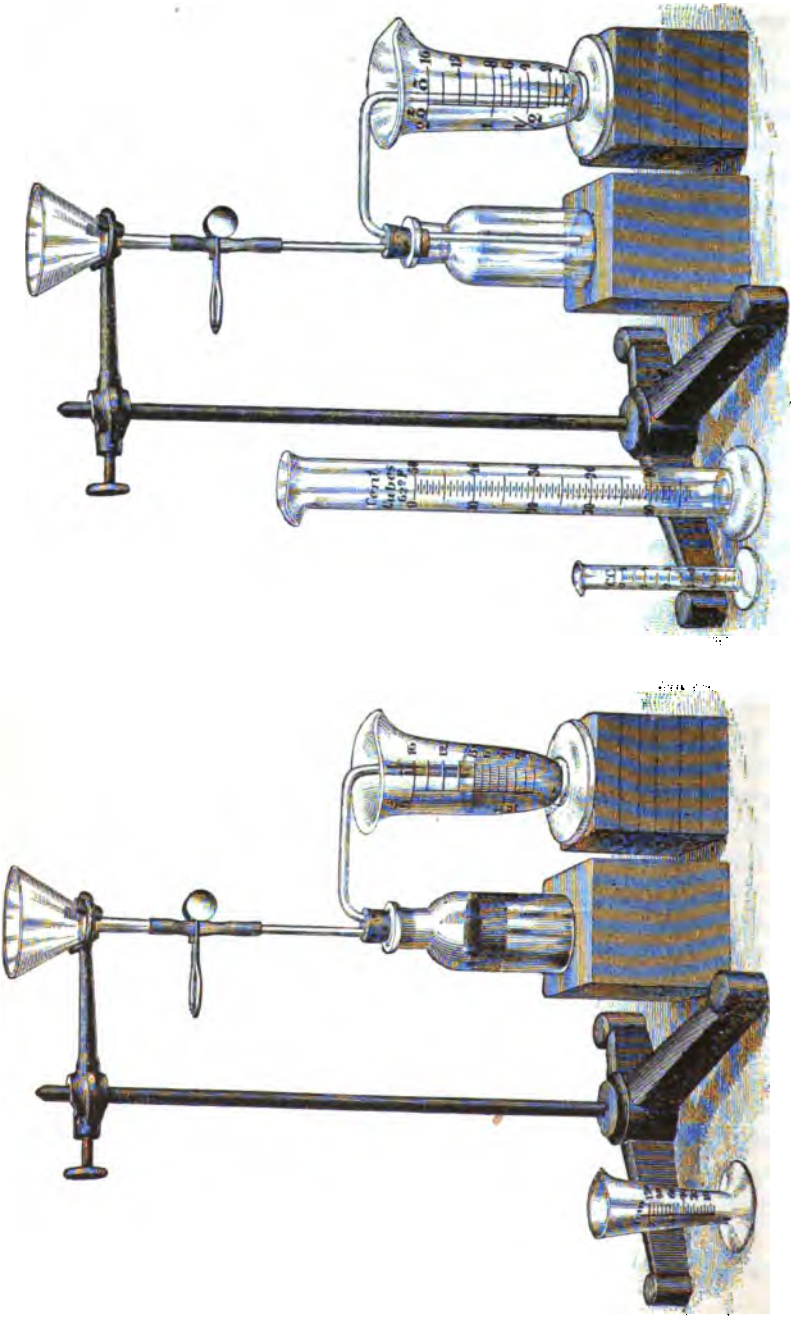
The chief value of the nitrometer lies in the accuracy of its measurements, and the ease and convenience with which these measurements are made, and any ruder form of apparatus for the application of this principle must necessarily sacrifice much of this accuracy; and the question is how much of this precision can be sacrificed in order to gain the wider sphere of usefulness. The nitrometer, carefully used, will measure the higher oxides of nitrogen in spirit of nitrous ether to within a half of one per cent. That is, to within a quarter of one per cent. above or below its indications. Now, if a simple apparatus be devised, from materials which are in the hands of a majority of physicians and pharmacists, or very easily procured at a small cost,—an apparatus that will measure to within one per cent. between the upper and lower extremes of its indications when used with educated, but not expert skill,—it is claimed that such an apparatus may have a very important value in medicine and pharmacy in discriminating between good and bad quality.

The chief difficulty overcome by the nitrometer is in the easy measurement of a liberated gas. This difficulty was measurably overcome by the writer in a very simple apparatus described and figured at p. 448, for the estimation of urea, wherein, instead of measuring a liberated gas, the liquid displaced by the gas was measured. This same device is now applied to the approximate measurement of the gas liberated in Mr. A. H. Allen's nitrometer process as described at p. 1195, et. seq.

The apparatus proposed for this rough assaying of spirit of nitrous ether is considered worthy of illustration by a cut, and is shown in two views on the following page. In the view on the right it is empty, to show the detail of its material and construction. On the left it is shown at the end of an assay process, when the measure is to be read off. In using the apparatus, however, it is a little more convenient to have the end toward the operator, rather than the side. Two sets of measures are shown,—the ordinary graduated measures of the U. S. P. and the French metric measures. These latter being narrow cylinders the measurements made by them are, of course, more accurate. But with care the others do fairly well.

The materials for construction are an apparatus stand of some kind, or a hole in a shelf,—a small glass funnel, half fluidounce capacity,—a section of rubber tubing with spring pinchcock,—a straight glass tube, and one bent twice at right angles with legs of equal length, of not over 2 millimetres or $\frac{1}{16}$ inch bore,—a cork with two holes for the tubes,—a vial of 60 c.c. or 2 fluidounces capacity, and some wooden blocks for stands. If the bent tube be over 2 millimetres the mercury is apt to run out of the external leg unless the end of the tube be kept immersed, and this is inconvenient.

For the best results in the measurements two graduated cylinders,—one of 10 c.c. and the other of 50 c.c., are required; or for ordinary use two common graduated measures,—one of 2 fluidrachms and the other of 2 fluidounces,—and these should agree on measurement, the one with the other. A dilute sulphuric acid, 2 in 6, and a strong solution of potassium iodide, 2 in 5, are used for the decomposition, exactly as with the nitrometer. The substance essential to the process, and least likely to be at hand, is about 2¼ avoirdupois pounds or 1.000 grams. of metallic mercury. Several fluids, including brine, were tried in endeavoring to avoid the use of mercury, but none would answer, and as mercury is not costly nor very difficult to obtain, and as the one charge is used over and over



Extemporaneous Substitute for Lunge's Nitrometer.

again indefinitely, the objections to it were not considered too great for the utility of the process. After each use the mercury is washed in a beaker, and is then used wet, or with a little water on the surface.

In charging the apparatus for a testing, the vial is filled so nearly full of mercury that when ten or twenty drops of water are put upon it the neck is full to the lip. Then when the cork is pushed into its seat the water overflows and the end of the cork takes the place of it, and comes nearly, or quite in contact with the surface of the mercury, and, the pinchcock being off, the mercury rises in the two tubes and fills a part of the horizontal portion of the bent tube. Then the funnel is connected with the vial by slipping on the lower end of the rubber tube, and the pinchcock being closed, about 1 c.c. of dry mercury is put into the funnel, and is slowly and cautiously let down into the vial, by slightly opening the pinchcock, until the bent tube is entirely filled with mercury, and some little has escaped into the 2 f ℥ receiving measure under the tube. When this little mercury is poured out and the measure replaced the apparatus is ready for the assay. There will be bubbles of air and drops of water in the straight tube, but they may be disregarded as within the sphere of unavoidable error. There must, of course, be no leaking at any of the connections, and should there be any leakage it is at once recognized by the mercury continuing to drop from the tube into the measure.

If the common U. S. P. officinal measures be used 1 f ʒ of the spirit of nitrous ether to be assayed is measured into the funnel and cautiously let into the vial by means of the pinchcock. Next the same quantity of the solution of potassium iodide is let in very slowly in the same way, and finally the same measure of the diluted sulphuric acid. This will make in all 3 f ʒ of liquid to be subtracted from the measure of the mercury in the receiving 2 f ℥ measure. As soon as the solution of the iodide is admitted the reaction begins, and if this be rapid, as it is with a strong spirit, the solution must be let in very cautiously and slowly to avoid the forcing of the gas up through the funnel. In 10 minutes the reaction is practically over, and the receiving measure may be taken away, and the quantity of mercury be read off. In taking this measure away almost all the mercury in the tube runs back into the vial, as it should do, since it should not be measured with that in the receiving measure. In reading off the measure the surface of mercury is found convex, with the convexity upward, and of course the level of the liquid is the reading line, and not where the metal touches the glass. Then the measure of the spirit taken for the assay, divided into the measure of mercury displaced by the gas, indicates the number of times the gas exceeds the spirit. If the mercury be 11 to 13 times the volume of the spirit taken the spirit will have contained about 5 p.c. of ethyl nitrite. If the volume be 2.2 to 4.2 times that of the spirit, this will indicate about 1 p.c. of ethyl nitrite, and in this same proportion for all volumes, and of course for all denominations of measuring systems, but the metric system is much the best, and the measuring vessels much the most accurate from their better graduation and much narrower surface.

Each per cent. of indicated ethyl nitrite is about equal to 1.86 p.c. of the total complex ethereal liquid in the spirit. That is, for each p.c. of ethyl nitrite the spirit will contain about .86 p.c. of other ethereal products of the distillation.

In washing out the apparatus after each rough assay it will be observed that the mercury which has been pushed through into the measure is clean and dry, and ready to be used over. That remaining in the vial is poured into a large beaker with the iodine solution, and is easily and conveniently washed by a current of water run upon it; the vial, of course, having been rinsed out in the same way, the clean mercury and water are poured back into it, the water overflowing as the mercury runs in. The mercury of one charge is of course just right for any number of subsequent trials, and when in the vial the neck will be left full of water, ready for the cork.

Eleven assays made with this apparatus and checked by the nitrometer, gave the following results:

In every case wherein this apparatus was used, the 1 fluidrachm taken was measured in the ordinary 2 f ʒ measure, as shown in the cut, and the displaced mercury in the 2 f ℥ measure, as shown, and when the measure came between the marks in the 2 f ℥ measure it was estimated by the eye. This being converted into fluidrachms, the 3 fluidrachms of liquid,—spirit, iodide solution and acid,—were subtracted, and the remainder divided by 2.2, for the percentage of nitrites. Then the mercury was poured from the measure into a narrow 50 c.c. cylinder, in which it could be more accurately measured, and the percentage calculated in the same way on this measure, assuming the fluidrachm to be 3.7 c.c. The two sets of results and differences are given in two sets of columns. Then the same spirit and the same reagents were used in the nitrometer at the same time, so that the temperatures of gas and liquid were the same. As will be seen, the differences,—and therefore the errors of this apparatus in excess of the errors of the nitrometer,—were, with a single exception, below .5 p.c. and were generally very much below this. It will also be seen that the plus and minus quality of the errors is fairly distributed.

TABLE No. 1.

Comparison of the Indications of the Nitrometer with the Indications of the Proposed Substitute for the Nitrometer for Roughly Testing Spirit of Nitrous Ether for Nitrites.

Samples of Spirit of Nitrous Ether.	NITROMETER.	NITROMETER SUBSTITUTE.				REMARKS.
		ORDINARY GRADUATED MEASURES USED.		GRADUATED CYLINDERS, METRIC MEASURES USED.		
	Indications Per cent.	Indications Per Cent.	Difference from Nitrometer.	Indications Per Cent.	Difference from Nitrometer.	
No. 1	5.135	4.772	.363—	4.500	.635—	Freshly made standard strength.
2	4.590	4.390	.200—	4.120	.470—	After being opened many times.
3	2.279	2.348	.069+	2.135	.144+	From commercial “ Con. Ether.”
4	2.396	2.500	.104+	2.342	.054—	“ “ “ “
5	2.342	2.386	044+	2.215	.127—	“ “ “ “
6	2.180	2.216	.036+	2.060	.120—	“ “ “ “
7	.450	.300	.150—	.371	.079—	Commercial Spirit marked U.S.P.
8	.378	.388	.010+	.427	.049+	“ “ “ “
9	.576	.570	.006—	.596	.020+	“ “
10	.405	.284	.121—	.315	.090—	“ “ marked U.S.P.
11	.693	.681	.012—	.709	.016+	“ “

It may be useful now to offer a review of some of the modern pharmacopœial processes for spirit of nitrous ether, in order to compare them, and bring out their principal points of merit or defect, with a view to a better understanding of the improved process which is to follow them.

PROCESS OF THE U. S. P. OF 1860.

A careful and critical application of this process, for the purposes of this paper, using one-fourth of the quantities, gave results which left little to be desired. The 4.875 troyounces of acid yields about 34 fluidounces, or 26 troyounces and 440 grains of finished spirit, of a s.g. of .837 at 15.6°C. which fairly stands the officinal description and tests given. Tested by the nitrometer three days after being made the 3 c.c. gave 37.9 c.c. of liberated gas,—equal to 12.6 times its volume, or 5.7 p.c. of nitrites, equal to about 10.6 p.c. of the complex ethereal liquid.

In the light of the experience had with this process before and since it became officinal, the quantity of alcohol distilled with the acid is about one-third too great, and this excess has to be distilled off before and after the proper reaction. But the objection to this is not very great here, as this excess is not lost, but only prolongs the time needed for the distillation and rectification. The greatest objection to the process is the rectification, which is wasteful of the ethers and quite unnecessary, if, instead, the ethers be washed with dilute solution of sodium carbonate as in the improved process to be proposed. Another serious objection in the light of recent experience is the omission to direct the use of iced-water and crushed ice in condensing.

PROCESS OF THE U. S. P. OF 1870.

A careful and critical application of this process was made for this paper, on the officinal scale of quantities. The 4.5 troyounces of acid here yield about 107 fluidounces or 80 troyounces of finished spirit, of a s.g. .824 at 15.6°C.

Tested by the nitrometer, three days after being made, the 3 c.c. gave 11.4 c c. of liberated gas,—equal to 3.8 times its volume; or 1.7 p.c. of nitrites equal to about 3.2 p.c. of the complex ethereal liquid,—more than 3 times the quantity of spirit of the 1860 process, and less than one-third the strength.

The process is not an inconvenient or difficult one to manage, but with care in managing the bath, so as to be prompt in checking the boiling at first, by the application of a cold bath, the whole of the nitric acid may be added before the heating. But it is contended that the sulphuric acid and copper are useless complications of the process,—that it is impossible to distill the prescribed quantity at or below the prescribed temperature, or at any temperature possible with a bath of boiling water. It is also held to be a defect in the process to omit both rectification and washing the object of which is to free the ethereal liquid distillate from acid and from water soluble products of the distillation. But by far the most objectionable feature of the process is the very large dilution of the ethereal liquid. In the process of 1860, the products of 4.875 troyounces of acid are diluted to give about 27 troyounces of finished spirit, while here the products of 4.5 troyounces of the same acid are diluted to 80 troyounces of finished spirit. That is, a smaller quantity of acid is made to produce three times as much finished spirit, and this without any officinal notice of a reduction in strength,—and without very much improvement, or any notice of change in the revision of 1880. The use of ice here, also, gives much better results.

The 1860 process describes its product as having a s.g. of. 837, and containing from 4.3 to 5 p.c. of its peculiar ether. The 1870 process of one-third the strength or less, describes its product as having the same s.g. and as containing 5 p.c. of its peculiar ether.

PROCESS OF THE U. S. P. OF 1880.

SPIRITUS ÆTHERIS NITROSI.

SPIRIT OF NITROUS ETHER.

[SWEET SPIRIT OF NITRE.]

An alcoholic solution of Ethyl Nitrite [$C_2H_5NO_2$; 75.—C_4H_5O,NO_3; 75], containing 5 per cent. of the crude Ether.

Nitric Acid, *nine parts*	9
Sulphuric Acid, *seven parts*	7
Alcohol.	
Distilled Water, each, *a sufficient quantity*	

Add the Sulphuric Acid gradually to *thirty-one* (31) *parts* of Alcohol. When the mixture has cooled, transfer it to a tubulated retort connected with a well-cooled condenser, to which a receiver, surrounded by broken ice, is connected air-tight, and which is further connected, by means of a glass tube, with a small vial containing water, the end of the tube dipping into the latter. Now add the Nitric Acid to the contents of the retort, and, having introduced a thermometer through the tubulure, heat rapidly, by means of a water-bath, until strong reaction occurs and the temperature reaches 80° C. (176° F.). Continue the distillation at that temperature, and not exceeding 82° C. (180° F.), until the reaction ceases.

Disconnect the receiver, and immediately pour the distillate into a flask containing *sixteen* (16) *parts* of ice-cold Distilled Water. Close the flask and agitate the contents repeatedly, keeping down the temperature by immersing the flask occasionally in ice water. Then separate the ethereal layer and mix it immediately with *nineteen* (19) *times* its weight of alcohol.

Keep the product in small, glass-stoppered vials, in a dark place, remote from lights or fire.

A clear, mobile, volatile and inflammable liquid, of a pale straw-color, inclining slightly to green, a fragrant, ethereal odor, free from pungency, and a sharp, burning taste. Sp. gr. 0.823 to 0.825. It slightly reddens litmus paper, but should not efferverse when a crystal of bicarbonate of potassium is dropped into it. When mixed with half its volume of solution of potassa, previously diluted with an equal volume of water, it assumes a yellow color, which slightly deepens without becoming brown, in twelve hours. A portion of the Spirit, in a test-tube half filled with it, plunged into water heated to 63° C. (145.4° F.), and held there until it has acquired that temperature, should boil distinctly on the addition of a few small pieces of glass.

If 10 Gm. of Spirit of Nitrous Ether be macerated with 1.5 Gm. of potassa for twelve hours, with occasional agitation, the mixture then diluted in a beaker with an equal volume of water, and set aside until the odor of alcohol has disappeared, then slightly acidulated with diluted sulphuric acid, and a solution of 0.355 Gm. of permanganate of potassium gradually added, the color of the whole of this solution should be discharged (presence of at least 4 per cent. of real Ethyl Nitrite).

Preparation: Mistura Glycyrrhizæ Composita.

This U. S. officinal process is a well constructed, easy and convenient one, and yields a fairly uniform product, though not in uniform quantity. But it is not the best that can be desired, for the following reasons: The sulphuric acid is absolutely useless, as was shown by the writer in 1856, and as now again proved by repeated trials with and without it, by examination of the product, —and by a long experience. As it has been abundantly proved that the presence of water in the product is the principal cause of the rapidity of the changes which occur in keeping, and as it is easy to get alcohol of a lower s.g. than .820, the alcohol used should be stronger and not above s.g. .815 at 15.6° C. Such an alcohol makes the very important difference of 2 p.c. less water out of a total of 9 p.c., and makes the preparation keep about 20 p.c. better. The quantity of alcohol directed is much too large. About 10 parts are required for the reaction, but to moderate this within manageable limits 16 or 17 parts instead of 31 are required. If much more than this be used, the excess will distill over before the reaction begins or after it is over, and will thus be wasted, and will much prolong the distillation. Beside this it will involve loss of ether in the washing process. If the nitric acid be added to the alcohol in the retort as directed, it will sometimes go to the bottom without sufficient admixture, and when there heated with but little alcohol, it occasionally sets up a reaction so violent as to be hard to control, even with cold water aspersion, and this always involves much loss by liberating the ether faster than it can be condensed. The acid should be added to the alcohol in a flask and be well mixed with it before being poured into the retort. The mixture is particularly liable to bumping and explosive boiling, and this involves the driving of gushes of ether through the apparatus uncondensed, and the carrying over of particles of the acid liquid in the retort. This is almost wholly avoided by having a very thin layer of broken glass on the bottom of the retort. With this the distillation is so comparatively steady, and so easily managed and controlled that no process should fail to direct the broken glass as an essential element. Beside, it causes the distillation to proceed, from first to last, at a lower temperature, as the operator will find to his cost if he undertakes to drop in the glass during the distillation, for then a single fragment will cause his charge to boil over. Another omitted direction is of equal importance. When the reaction in the retort is fairly established, and before it becomes very active, the hot water bath must be withdrawn, and cool water must be ready to be applied, to check the rapidity of the boiling, because no ordinary condensing apparatus can take care of the ether vapor when so rapidly liberated. If the 31 parts of alcohol be used the temperature always rises above 80°C. before there is much distillation, and often will gradually go up to 85° before the excess of alcohol is off, and the reaction commences. The reaction is easily seen to be different from the simple boiling off of the excess of alcohol, and it is marked by the gradual change of the boiling liquid from colorless to yellow and by the occurrence of faint orange vapors in the retort. This is the time for taking away the hot bath, and the temporary application of cooler water if needed, and during this active stage of the reaction the temperature will fall to 70°C. or below this, and will remain low until the water of the hot bath is again applied to keep the distillation up to a proper rate, and the water will nearly boil by the time the temperature reaches 82°C. The reaction does not cease at this temperature, but the product received from 82° to 90°C. is weak alcohol with so little ether in it that it should be rejected as directed in the process. When the distillate is poured into the 16 parts of ice-cold water and shaken with it, the water washes out the alcohol which has come over with the ether, making with the water a dilute alcohol, which in proportion to its greater or less alcoholic strength will dissolve more or less of the ether. This ether so dissolved is thrown away, and hence another important reason why the taking so large an excess as 31 parts of alcohol is a mistake. This washing does not wash out all the acids from the ether as intended, though it might well do this if it contained a little sodium carbonate ; but is nevertheless a very good and very important step of the process, because it tends to make the ethereal product fairly uniform in character when it comes to be diluted. Then the final step of diluting this product with a given number of times its weight of alcohol is a very good provision, because however imperfect or wasteful may have been the process, or its management, the quality of the finished product will be fairly uniform,—the quantity yielded, only, being deficient. But the dilution to the extent of 19 times its weight is a mistake. This dilution makes a finished product containing 5 p.c. of the washed ether, and the statement is made that it should contain at last 4 p.c. of real ethyl nitrite, which is far from being the case under any possible management.

This process was applied many times for the purposes of this paper, on a scale of half a troyounce to each part,—a scale well adapted to the use of the pharmacist. This scale requires 4.5 troyounces of nitric acid and 15.5 troyounces of alcohol for the distillation. Nitric acid of s.g. 1.42 is difficult to get in the market. But an excellent quality of acid of about s.g. 1.4105 at 15.6°C. is easy to get at a moderate price, and as the difference is only about 1 p.c. in strength this acid was accepted for these distillations. The alcohol was brought to the officinal strength as nearly as practicable,—that is, to s.g. .8204 at 15.6°C. After some experience, on this scale, with these materials, a critical trial of the U. S. P. process was made and yielded the following results,—these results being above the general average, because broken glass was used in the retort, and a very thorough condensation was effected by means of ice.

The ethereal distillate received weighed.	8 troyounces and	128 grains
This when washed with the ice-cold water was reduced to...........	2 troyounces	466 grains.
Showing a loss of..........	5 troyounces	142 grains.

This loss was, of course, mainly alcohol, abstracted by the water, and the 8 troyounces of water with the 5 troyounces of alcohol forms a spirit strong enough to dissolve a very important proportion of the ether, which is then discarded with the washings.

But these washings weighed	12 troyounces and 455 grains.
when they should have weighed,—water, 8 troyounces. plus loss to the water in washing 5 troyounces and 142 grains.	
or a total of..............	13 troyounces and 142 grains.
Showing that 167 grains of the mixture of water, alcohol and ethereal liquid, which constitute the washings, must have been taken up by the washed ether.	167 grains.

The s.g. of the washed ether was .9077 at 4°C. and .8931 at 15.6° C., while the s.g. of pure ethyl nitrite, see ante, is .9177 at 4°C. and .8977 at 15.6°C.

The washed ether=2 troyounces and 466 grains, diluted with 19 times its weight of alcohol, s.g. .8204 at 15.6°C., yielded 56 troyounces and 214 grains of finished officinal spirit of nitrous ether of a s.g. of .8330 at 4°C. or .8238 at 15.6°C.

This spirit subjected to the nitrometer test gave, from 3 c.c., 18.8 c.c. of liberated gas, or about 6.2 times its volume, or (18.8÷6.66=) 2.82 p.c. of nitrites. Then as it actually contains 5 p.c. of the complex ethereal liquid, it follows that (5—2.82=) 2.18 p.c. of this ethereal liquid is neither ethyl nitrite nor any other nitrite.

This shows that at its very best the present officinal process yields a spirit containing 5 p.c. of its peculiar and characteristic ethereal liquid, but only 2.82 p.c. of real ethyl nitrite when freshly made. That is, about 1 part ethyl nitrite in 1.77 parts of the complex ethereal liquid by the process.

The washing of the ethereal distillate with a prescribed quantity of ice-cold water, is, as has been said, a very useful and important step peculiar to this process, because it renders the washed ethers fairly uniform in character and quality, before dilution with a prescribed proportion of alcohol. But the washing is doubtless a wasteful proceeding, and the washings require to be noticed, especially in their relations to the therapeutic uses of spirit of nitrous ether, to be referred to farther on. These washings have all the sensible properties of good spirit of nitrous ether, in a high degree, and yet give no indications of ethyl nitrite by the nitrometer. They consist of the 8 troyounces of very cold water, plus 5 troyounces of distillate that is washed out. A very large proportion of this 5 troyounces of distillate lost to the water, is undoubtedly alcohol, converting the water into a dilute alcohol, and in such a dilute alcohol ethyl nitrite is soluble to a very considerable extent. The reason why it is not present to the nitrometer is not known. That portion dissolved may be decomposed by the water, but if so, why should not a very large proportion, or all of it, be so decomposed? And if decomposed, what becomes of the products of the decomposition?

When ethyl nitrite,—and presumably when spirit of nitrous ether is decomposed by much water, gaseous nitric oxide, NO, is liberated. This gas on contact with air is at once converted into nitrogen tetroxide, NO_2 red fumes. This resulting gas or vapor in contact with much water, splits into nitric oxide, NO, and nitric acid, $H\,NO_3$. The nitric oxide, NO, again oxidized by the air to red fumes of NO_2 again splits by the water, and so on until all is converted into nitric acid. (See Treatise on Chemistry, Roscoe and Schorlemmer, vol. I., p. 429.)

Now, when a definite volume of solution of ethyl nitrite, or a spirit of nitrous ether indicating 5 p.c. or more of ethyl nitrite, was let into the nitrometer on top of the brine, and was followed by successive equal volumes of cold water, the first volume of water liberates but little gas. The second liberates more and the third liberates much more, and the gas increases for several hours. This gas should be nitric oxide, NO, and actually about five-sixths of it is absorbed by cold solution of ferrous sulphate. But on letting into it about half its volume of air it is not converted into red fumes as it should be, but remains colorless, and is not absorbed by the water, so that the reactions as above quoted are apparently not explanatory of these reactions, and the chemistry of them is too difficult for the writer.

PROCESS OF THE BRITISH PHARMACOPŒIA.

The British Pharmacopœia of 1864, p. 323, prepared its Spiritus Ætheris Nitrosi by distilling together nitrite of sodium, sulphuric acid and rectified spirit, but gave no characteristics nor tests. In

1867, p. 293, the change was made to the process which is characterized by the use of metallic copper. In 1885 this process is continued with a few slight changes. When first published in 1867 the writer had some experience with this copper process, both on the large and the small scale, but it was soon abandoned for a return to the then U.S.P. process. And as the reasons for giving it up are now beyond recall, it is thought worth while again to make a critical trial of it.

The present process,—British Pharmacopœia, 1885, p. 377,—is as follows, the explanatory figures in parenthesis being added by the writer:

"SPIRITUS ÆTHERIS NITROSI.

SPIRIT OF NITROUS ETHER.

[SYNONYM. SPIRITUS ÆTHERIS NITRICI.]

A spirituous solution containing nitrous compounds, aldehyd, and other substances. It may be obtained as follows:—

Take of

Nitric Acid ....3 fluidounces. (s.g. 1.42 at 15.6°C. 85.2 c.c.=119.2 grammes, or 1840 grains=3 troyounces 400 grains.)

Sulphuric Acid............2 fluidounces. (s.g. 1.843 at 15.6°C. 56.8 c.c.=103.6 grammes, or 1598.8 grains=3 troyounces 158.8 grains.

Copper, in fine wire (about No. 25) 2 ounces. (56.7 grammes, or 875 grains.)

Rectified Spirit............a sufficiency. (Alcohol of s.g. .838 at 15.6°C., or about 84 p.c. by weight.)

To one pint (20 fluidounces) of the spirit add gradually the sulphuric acid, stirring them together; then add, in the same way, two and a half fluidounces of the nitric acid. Put the mixture into a retort or flask, into which the copper has been introduced, and to which a thermometer is fitted. Attach now an efficient condenser, and applying heat gently, let the spirit distill at a temperature commencing at 170°F.—76.7°C.—and rising to 175°F.—79.4°C.—not exceeding 180°F.—82.2°C.—until twelve fluidounces have passed over and been collected in a bottle, the latter and the condenser being kept cool with ice-cold water; then withdraw the heat, and having allowed the contents of the retort to cool, introduce the remaining half-ounce of nitric acid, and resume the distillation as before, until the distilled product has been increased to fourteen fluidounces. Mix this with two pints of the rectified spirit or as much as will make the product correspond to the nitric oxide test alluded to in the following paragraph. Preserve the product in thoroughly well closed vessels.

Characters and Tests. Transparent and nearly colorless, with a very slight tinge of yellow, mobile, inflammable, of a peculiar, penetrating, apple-like odor, and sweetish cooling sharp taste. Specific gravity 0.840 to 0.845 (at 15.5°C.). It does not effervesce, or only feebly, when shaken with a little bicarbonate of sodium. When agitated in a test-tube with a strong solution of sulphate of iron, if a few drops of strong sulphuric acid are then poured down the side of the tube, a deep olive-brown or black zone is produced, widening as the tube is gently shaken. Tested as described in the *Pharmaceutical Journal,* 3d series, vol. XIII., page 63; or, vol. XV., page 101; or, vol. XV., page 673, it should yield, at the ordinary temperature, – 60°F., 15.5°C.—and pressure—30 inches or 760 millimetres of mercury,—and when freshly prepared, seven times its volume of nitric oxide gas; and even after it has been kept some time and the vessel containing it has occasionlly been opened, it should yield not much less than five times its volume of the gas.

Dose.—½ to 2 fluidrachms."

This process with half these quantities was carried out with critical care and accuracy, using a water-bath for distilling, and crushed ice for cooling, and using a final flask containing alcohol to absorb the gas which might escape the receiver imbedded in the crushed ice,—the flask also being in an ice-bath. The only departure from the process was in the use of alcohol of a s.g. of .8148 at 15.6° C.,—that is, a spirit of 93 p.c. instead of 84 p.c. The use of an alcohol so much stronger should lower the boiling point and increase the reaction. This latter it did, but the prescribed quantity of distillate could not be obtained under the prescribed temperature of 82.2°C., and when carried to 88°C. the first distillate was still two fluidounces short in measure. After the addition of the last portion of nitric acid, however, half an ounce more than the prescribed quantity was received below 88°C., so that the total distillate was one and a half fluidounces short. The reaction began much below the prescribed temperature, as was to be expected,—and became so strong that the hot bath had to be removed, and a cooling bath to be applied several times to moderate the reaction, and avoid loss of uncondensed ether. But the boiling was kept very steady and the process was very successful. After the receiver was detached another was applied and the distillation was continued from 88° up to 91°C., the product being a considerable quantity of alcohol with a very litle nitrite. One of the disadvantages of the process is the loss of this alcohol, but this cannot be avoided if the process be followed, because the excess of alcohol is needed to moderate the reaction by dilution.

The first distillate, below 88° C., meas.	149 c.c.	(5 f ℥)	and wgd.	129.8 grams.
The second " " " "	47 "	(1.6 f ℥)	"	39.7 "
Total......	196 "	(6.6 f ℥)	"	169.5 "

The final flask, to absorb the vapors which escaped the receiver, contained at starting 125 c.c.=100 grams. of alcohol, and at the end the weight had increased to 104 grams. This alcohol was taken as a part of the pint (20 fluidounces) of alcohol with which, by the process, the total distillate was diluted to make the finished spirit of nitre. The finished spirit measured about 764 c.c. or nearly 27 fluidounces,* and weighed 623 grams., or nearly 22 avoirdupois ounces.

The s. g. at 15.6°C. as made with this 93 p. c. alcohol is .8278. In other respects it accords fairly well with the description, excepting in the test by nitrometer.

Tested by the nitrometer 3 c.c. gave 36 c.c. of gas, or 12 times its volume instead of 7 times as prescribed by the Br. P. Then as 6.66 c.c. of gas from 3 c.c. of spirit correspondend to about 1 p. c. of ethyl nitrite, it follows that this spirit contains (36÷6.66=) 5.4+p. c. of ethyl nitrite, as freshly made, by the Br. P. process, from 93 p.c. alcohol, with very thorough condensation by iced-water and ice. The additional quantity of alcohol required to dilute it to the Br. P. strength of yielding 7 times its volume of gas would not be easy to determine, but when so diluted the spirit would contain about 3.15 p.c. of ethyl nitrite.

The distillate above 88°C. and below 91°C., when distillation practically ceased,—gave an indication by nitrometer of about .2 p. c. ethyl nitrite, and had the odor and taste of commercial spirit of nitre. This distillate, which is discarded by the process, amounted to about 2.5 fluidounces.

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* The "fluidounce" of the British Pharmaçopecia is 437.5 grains of water or 28.397 c.c. while the fluidounce, wine measure, of the U. S. P. is 455.7 grains of water or 29.52 c.c.

As the Br. officinal distillate is not washed, and is too much diluted with the excess of alcohol to be washed to advantage, and therefore cannot be easily compared with products that are washed, it became necessary to repeat the process in such a way that the complex ether might be washed. This was done, using the full quantities of the Br. P., except that only 14 fluidounces of 93 p. c. alcohol were distilled with the acids and copper, instead of 20 fluidounces of 84 p. c.,—a bath of cold water being used to moderate the reaction,—which reaction started spontaneously, from the heat developed in mixing the materials. Iced-water and crushed ice were copiously used in condensing the vapors and a water bath was applied for heating, after the spontaneous boiling diminished. More than half of the distillation went on spontaneously, several degrees below the prescribed temperatures, but toward the end the heating was applied up to 88°C.

The total distillate measured 220 c.c. and weighed 195.4 grams.,—or, if the 3.2 grams. increase in weight of the alcohol in the end flask be added,—223.6 c.c. and weighed 198.6 grams. But this latter could not be included in the washing, and therefore was discarded.

The 220 c.c.=195.4 grams. of distillate was washed by being repeatedly and vigorously shaken with 200 c.c. of ice-cold distilled water, and the liquids then separated.

The ethers then measured 97 c.c. and weighed 85.38. grams.

The washings then measured 315 c.c. and weighed 303.15 grams. having increased by 115 c.c., or 103.15 grams.—the ethers having decreased by 123 c.c., or 110.02 grams. The discrepancies are to be accounted for by contraction, and by water taken up by the ethers. The residue in the retort and the washings were both tested by the nitrometer and gave no indication of nitrites.

The 85.38 grams. of washed ethers had the following specific gravities :

At 4°C. or 39.2°F.	.9053.		
" 15.6°C. or 60°F.	.8918.	Difference	.0135.
" 25°C. or 77°F.	.8812.	"	.0106.

In no other instances could the s.g. of the washed ethers be taken at 25°C. on account of the low boiling point, but with these ethers there was no difficulty.

These trials afford the desired opportunity of comparing the results of the distillation of nitric acid and alcohol with and without the use of sulphuric acid and copper.

It will be shown farther on that when 5 troyounces or 2400 grains of nitric acid of a s.g. 1.42 at 15.6°C. are distilled with 8.5 troyounces or 4080 grains of alcohol of s.g. .8148 at 15.6°C. at temperatures up to about 88°C., and the distillate is well washed with about an equal volume of ice-cold distilled water, the resulting washed ethereal liquid is pretty uniformly about 2000 grains, and the s.g. of this is about .8965 at 15.6°C. That this ethereal liquid, or complex ether, when diluted with 11 times its weight of the same alcohol, gives about 24000 grains of a spirit of nitrous ether which tests by the nitrometer about 5.35 p.c. ethyl nitrite. Then as this spirit contains 8.33 p.c. of the complex ethereal liquid, and gives a nitrometer indication of 5.35 p.c. of ethyl nitrite, it follows that by that process about five-eighths of the complex ethereal liquid is ethyl nitrite.

It is now shown that when 1840 grains of the same nitric acid is distilled with 4960 grains of the same alcohol, with the addition of 1599 grains of sulphuric acid and 875 grains of copper, at temperatures up to about 88°C. under conditions of condensation, etc., which were practically the same ; and the distillate is washed in the same way, the washed ethereal liquid has a s.g. of .8918 at 15.6°C. and weighs 1380 grains. That this ethereal liquid when diluted with 11 times its weight of the same alcohol gives about 15810 grains of a spirit of nitrous ether which tests by nitrometer 3+p.c. of ethyl nitrite. Then as this spirit contains 8.33 p.c. of the complex ethereal liquid, and gives a nitrometer indication of 3 p.c. of ethyl nitrite, it follows that by this Br. P. process about three-eighths of this complex ethereal liquid is ethyl nitrite.

In the first experiment with the Br. process, wherein it was critically followed, excepting only that 93 p.c. alcohol was used instead of 84 p.c., the 6.6 fluidounces of total distillate weighed 169.5 grams. or 2616 grains. As deduced from the results of the second experiment with this process this 2616 grains should consist of about 1143 grains of the complex ethers and 1473 grains. of other liquids soluble in water, and doubtless chiefly alcohol. If it be taken as alcohol of dilution, then it must be added to the 20 fluidounces or 7086 grains of alcohol of final dilution, making the total alcohol of dilution (1473+7086=) 8559 grains, and this is about 7.5 times the weight of the complex ethers, had these been washed out. This limited dilution therefore is the reason why this spirit indicates as high as 5.4 p.c. of ethyl nitrite. Had it been diluted with about 11 times the weight of the complex ether it would have indicated by the nitrometer about 3.6 p.c. of ethyl nitrite. The Br. P. requires that when tested by the nitrometer it should give 7 times its volume of the gas,—or, from 3 c.c. it should give 21 c.c. of gas. Then as when 3 c.c. is taken for the testing, 6.66 c.c. of gas indicates 1 p.c. of ethyl nitrite, 21 c.c. would indicate (21÷6.66=) 3.15+p.c., this being what the Br. P. requires. Therefore the results of this first experiment are found to be practically in fair accord with those of the second.

The conclusion reached is, that 2400 grains of nitric acid distilled with alcohol gave a spirit amounting to 24000 grains, and indicating 5.35 p.c. of ethyl nitrite. And that 1840 grains of nitric acid distilled with sulphuric acid, copper and alcohol, gave 15810 grains of a spirit, indicating 3+p.c. of ethyl nitrite.

Had the same quantity of nitric acid been used in the second case as in the first, the amount of finished spirit yielded would have been (as 1840 : 15810 : : 2400 :) 20622 grains of 3 p.c. spirit against 24000 grains of 5.35 p.c. spirit.

The two products when submitted to the other tests were found to be practically alike. Both had insignificant traces of aldehyd, but that by the Br. process had least. That by the Br. process was slightly but decidedly acid to neutral litmus paper, while the other was neutral.

Only approximative accuracy is claimed for this comparison of processes, but the difference in favor of the simple distillation of nitric acid and alcohol is so great as to be far outside of the limit of probable error, either in the management of the processes, or the conversion of the confused systems of weights and measures.

IMPROVED PROCESS.

An improved process based upon the present officinal one is now to be proposed and urged upon the Committee of Revision for 1890; and in this it is aimed to get, in ordinary educated practice, a finished product that when freshly made will test about 5 p.c. of ethyl nitrite by nitrometer. This process is as follows :

SPIRITUS ÆTHERIS NITROSI.

SPIRIT OF NITROUS ETHER.

[SWEET SPIRIT OF NITRE.]

An alcoholic solution of a complex ethereal liquid containing about 8.33 per cent. of the complex ethereal liquid, and giving, when freshly made, a nitrometer indication of 5 per cent. of ethyl nitrite [$C_2H_5NO_2$; 75].

Nitric Acid, s.g. 1.42, *twenty parts*	20
Alcohol, s. g. .815, *a sufficient quantity.*	
Sodium Carbonate, *one part*	1
Stronger Water of Ammonia.	
Distilled Water, each, *a sufficient quantity.*	

Weigh into a flask, first 34 parts (8.5 troyounces, or 11 f℥ of Alcohol, and then 20 parts (5 troyounces or 3.71 f℥) of Nitric Acid, and having shaken them well together, pour the mixture, without any splashing, into a tubulated retort or flask of double the capacity of the contents, containing fragments of broken glass. Connect this, air-tight, with a well-cooled condenser of great capacity, to which a receiver, surrounded by finely crushed ice, is connected air-tight. Connect this receiver, by means of a bent glass tube, with a flask surrounded by crushed ice, containing 16 parts (4 troyounces or 5.18 f℥) of alcohol, the glass tube to pass loosely through a cork in the neck of the flask almost to the surface of the alcohol. Apply to the retort a hot water-bath, so arranged that the bath may be quickly removed, and then heat rapidly until the liquid boils briskly. Then remove the bath, pour out a half to two thirds of the hot water and add cold water so that the bath may be about 55°C. or 131°F. As the boiling becomes too rapid for effective condensation, apply the cooled bath, by hand, to the retort for a few moments, from time to time, so as to keep the boiling within the capacity of the condensers. When this checking is no longer needed, heat the bath up again, and have it ready to reapply when the boiling becomes too slow. Then reapply the bath and distill until the rate is reduced to slow dropping, and the residue in the retort is reduced to about 6 parts.

Disconnect the receiver and pour the contents into a flask containing 32 parts of ice-cold water in which the sodium carbonate has been dissolved before cooling. Close the flask and shake the contents vigorously and repeatedly, keeping down the temperature by immersing the flask occasionally in ice-water. Then separate the ethereal layer and mix it immediately with eleven times its weight of alcohol, taking the contents of the flask at the end of the condensing apparatus as a part of the alcohol of dilution.

Finally add stronger water of ammonia, a few drops at a time, until the finished spirit turns neutral litmus paper to a purple tint.

A transparent, volatile, inflammable liquid, of a pale yellow color and fragrant ethereal odor,—pungent, but free from acridity,—and having a sharp, burning taste. Sp. gr. at 15.6°C. or 60°F. .821 to .823. At 25°C. or 77°F. .815 to .817. If unopened, or but little exposed to light and air, it turns neutral litmus paper bluish for two months after being made, and for at least two months more fails to redden blue litmus paper. When one volume of Solution of Potassa is mixed with one volume of water, and then with two volumes of the spirit of nitrous ether, the mixture assumes a yellow color, which, in twelve hours, deepens without becoming brown (limit of aldehyd.)

When 3 c.c. of the Spirit recently made, or well kept, is tested by the nitrometer it should give not less than 11 times its volume, or more accurately 33.3 c.c. of liberated gas, which is equal to about 5 per cent. of ethyl nitrite. Any spirit which by age, or by being badly kept, yields less than 8 times its volume of gas, which is equal to about 3.5 per cent. of ethyl nitrite, should be rejected.

Spirit of Nitrous Ether was made by the above formula and process many times, the parts of the formula being taken as quarters of the troyounce (120 grains), the quantities actually used being given within brackets in the formula,—and the process was found to be easily managed, and to give fairly uniform results.

The 5 troyounces or 2400 grains of nitric acid reacting with the prescribed alcohol according to the explanatory equation given by authorities in general ($2C_2H_6O+HNO_3=C_2H_4O+C_2H_5NO_2+2H_2O$)—requires for the reaction about 5.446 troyounces, or 2615.4 grains of the 93 p.c. alcohol, and should yield about 5 troyounces and 27 grains, or 2427 grains of ethyl nitrite,—1423 grains, or nearly 3 troyounces of aldehyd and 1165 grains, or nearly 2.43 troyounces of water.

This explanation of the reaction, however, is not accepted by this writer, because the s.g. and other properties of the product will not permit it. There is no such proportion of aldehyd ever present, while several other products are present instead. The product is a complex ethereal liquid of unknown, but, as judged by its properties, of fairly uniform composition, about five-eighths of which is ethyl nitrite. And this ethyl nitrite is in a proportion so nearly uniform that the quantity present from this process, as indicated by the nitrometer, may be assumed as a practically fair representative of the total complex product in the proportion of 1 part ethyl nitrite in 1.66 parts of total ethereal product.

If nitric acid and alcohol are distilled in about the proportions above given as being theoretically equivalent, that is, 5 of acid to nearly 5.5 alcohol, the reaction is so rapid as to be controlled with difficulty, and a fairly good condensation of the vapors is impracticable. Therefore the proportion of alcohol must be increased until by dilution it renders the reaction manageable. If increased too much, however, as in the U. S. P. process, much of it will distill over before the reaction begins, or after the active part of it is over, thus wasting the time and the alcohol. The proper proportions for prompt and easily manageable reaction between acid and alcohol of the prescribed strength are 5 acid to 8.5 alcohol, and these proportions were reached by many trials of both more and less alcohol.

In making the mixture for distillation the acid must be added to the alcohol, because then the acid is diluted too quickly to admit of spontaneous reaction. But if the alcohol be added to the acid, spontaneous reaction is liable to occur before sufficient alcohol is mixed with the acid. The mixture should always be made in a flask, and not in the retort, and be well shaken before being poured into the retort, because if mixed in the retort it cannot be shaken, and the acid is liable to go to the bottom too little diluted, and there set up a spontaneous reaction. The mixture should be poured into the retort without splashing, because if drops are splashed up onto the dome of the retort or into the neck, they are carried over with the distillate.

If the acid be weak, as is generally the case with that found in this market, the quantity is to be increased, but if less than s.g. 1.38 at 15.6°C. (67 p.c.), it should not be used, because it introduces too much water. And for this same reason weak alcohol should not be used. Good acid is easily obtainable of a s.g. 1.406 to 1.409 at 15.6°C., and such an acid was used in all these investigations, and 5 troyounces and 86 grains were used as the equivalent of 5 troyounces of acid of s.g. 1.42.

Alcohol under the names of neutral spirit or cologne spirit can often be had of s.g. .8135 at 15.6°C., or 93.5 p.c., and such is to be preferred when obtainable. But it can always be had of s.g. .815, or 93 p.c., and such was used in all these trials, and 8.5 troyounces of this, measures 324.7 c.c., or just 11 fluidounces.

The distilling and condensing apparatus is very simple and should be of ample size or capacity, because even with the indispensable broken glass in the retort, the boiling is occasionally irregular or explosive, frothing up in the retort so as to go over into the condenser if the retort be too small. A Liebig's condenser with thin glass tube connected with the large neck of a tubulated receiver, by means of a large cork, so that the rate of distillation can be seen,—makes a very convenient arrangement. A glass tube bent twice at right angles, with a short and a long leg, has the short leg fitted tightly by a perforated cork into the tubulure of the receiver, while the long leg passes loosely through a cork in the mouth of a pint flask containing the 4 troyounces of alcohol, reaching very nearly to the surface of the alcohol. If it should enter the alcohol this will be surely drawn back into the receiver every time the boiling is checked during the distillation. The receiver and this final condensing flask should each be placed in a suitable vessel, so that finely crushed ice can be so piled around them as to cover them entirely, throughout the distillation, and should the distillation become too rapid for the condensers, it will be known by the strong odor of the vapor escaping from the flask. All joints excepting the last one should be made quite tight with wet bladder. The condensation is very much improved by having the whole beak of the retort wound with a strip of cotton cloth, and then by dropping cold water upon the upper part of this by means of cotton wick syphons from a vessel of iced-water. It is convenient and instructive, but not essential, to have a thermometer fitted into the tubulure of the retort by a tight cork, the bulb being very near the bottom, and this was the arrangement for these trials. A water-bath not much larger than the retort bottom is held in place by a ring of an apparatus stand, so that the water of the bath is about on a level with the liquid inside the retort. The temperatures prescribed in the various officinal processes, as not to be exceeded are to be disregarded as no of importance,—at least when strong alcohol is used in the process and a water-bath for heating and cooling, because, then too high a temperature is next to impossible. And, a water-bath should always be used, because a naked flame for alcoholic and ethereal distillations, from glass vessels, is very unsafe.

Everything being ready and a good stream of cold water going through the Liebig's condenser, the water-bath is heated by a lamp. By the time the temperature of the liquid in the retort reaches 40°C. or 104°F. streaks of condensed vapor are seen in the retort, and a very small quantity of colorless liquid drops into the neck of the receiver. Then as the temperature reaches about 70°C. or 158°F., the colorless liquid acquires a greenish yellow tint, indicating the beginning of the proper reaction, and columns of very fine bubbles arise from a few of the angles of the broken glass. At about 80°C. or 176°F. the liquid becomes more distinctly yellow, the columns of bubbles increased in number and size, and nearly colorless liquid, chiefly alcohol, distills over in slow dropping. At about 84°C. or 183.2°F. the reaction is fairly established, and true boiling begins at about 87°C. or 188.6°F., with distillation at the rate of moderately fast dropping. Within one or two minutes more the boiling becomes quite active and the distillation rate is very fast dropping or an interrupted stream, with a temperature of about 88°C. or 190.4°F. The lamp and the water-bath are then removed and the water of the bath is reduced to about 55°C. or 131°F. By the time this is done the boiling will have become too rapid for the condensers, and a pretty strong odor of the uncondensed vapor will be noticeable, escaping from the flask at the end of the apparatus. The cooled water-bath is then applied, by hand, to the retort for 15 or 20 seconds, and this reduces the rate of distillation to rapid dropping. Within a few minutes, however, the more rapid rate is resumed, and then the cooled bath is again applied; and this is repeated some five or six times, at increasing intervals, until a time is reached when the boiling and distillation first become steady for a time, and then begin to diminish. During this time the bath has been again heated to near boiling, on a separate stand, and when the rate of distillation has diminished to a moderate dropping, the hot bath is again applied to the retort, and soon after that the lamp is placed under the bath.

When the lamp and water-bath were first removed the temperature in the boiling liquid began to fall, and from 88°C., the highest point, it fell to about 75°C. or 167°F., when the hot bath was reapplied. It then began to rise again and went steadily up to the end.

The distillation is continued until the rate is reduced to very slow dropping, when very little liquid is left in the retort and the process is finished, and by this time the temperature will have reached about 96°C. or 204.8°F. The entire distillation occupies from an hour and a half to two hours.

During the distillation the 32 parts (8 troyounces) of distilled water will have been weighed in a flask, of about four times the capacity, and the 1 part (120 grains) of sodium carbonate will have been dissolved in this water, and the flask set in a bath of ice and water.

The contents of the receiver in 5 consecutive trials gave measures and weights as follows :

1st.	337	c.c.,	weighing	9	troyounces and	300	grains.
2d.	340.1	"	"	9	" "	362	"
3d.	340.	"	"	9	" "	366	"
4th.	342.	"	"	9	" "	380	"
5th.	346.	"	"	9	" "	460	" a critical trial.

These were poured into the ice-cold solution of sodium carbonate, and vigorously shaken six times, then transferred to a separator, and the washings drawn off closely.

The washed compound ether and the washings then measured and weighed as follows :

	ETHER.					WASHINGS HAD GAINED.			
1st.	130 c.c.	3	troyounces and	373	grains.	5	troyounces and	189	grains.
2d.	133 "	3	" "	411	"	5	" "	216	"
3d.	127 "	3	" "	318	"	5	" "	316	"
4th.	131 "	3	" "	376	"	5	" "	264	"
5th.	131.2 "	3	" "	387	"	5	" "	340	"

That the sum of the weights here do not reach the weights of the first table by 218., 215., 212., 220., and 213 grains is due, first, to loss in manipulating the very volatile ether ; and, second, to loss of carbonic acid from the sodium carbonate.

The washings contained almost all the alcohol that escaped decomposition,—and this, of course, is wasted,—contained very small quantities of several sodium salts,—were quite yellow from aldehyd resin, and had a very strong odor and taste of spirit of nitrous ether, but when tested by the nitrometer gave no indication of nitrites.

The washed compound ethers were very yellow in color, neutral to neutral litmus paper, and had the following specific gravities :

1st.	at 4°C.	or 39.2°F.	.9133.—	at 15.6°C.	or 60°F.	.8986.	Difference	.0147
2d.	at "	"	.9108.—	at "	"	.8964.	"	.0144
3d.	at "	"	.9110.—	at "	"	.8966.	"	.0144
4th.	at "	"	.9106.—	at "	"	.8960.	"	.0146
5th.	at "	"	.9110.—	at "	"	.8965.	"	.0145

The s.g. at 25°C could not be taken on account of the low boiling point of the ether. The s.g. of pure ethyl nitrite at 4°C. or 39.2°F. is .9177. At 15.6°C. or 60°F. by deduction is .8977. Difference, .0200.

The 16 parts or 4 troyounces of alcohol in the flask connected with the receiver increased in weight as follows, in the successive trials, 201, 215, 251, 208 and 208 grains, and this gain was doubtless ether, which, without the flask, would have been lost. It is, therefore, assumed that these gains should be added to the washed ethereal products, and when so added they bring the respective amounts up to,—for the 1st.—4 troyounces and 94 grains.

2d.—4 " " 146 "
3d.—4 " " 89 "
4th.—4 " " 104 "
5th.—4 " " 115 "

showing the totals to be very fairly uniform.

Now when 129 c.c., weighing 3 troyounces and 277 grains, of the washed ether* was diluted with 11 times its weight of alcohol, using the contents of the end flask as a part of this alcohol, it gave 1634 c.c. or 55.3 fluidounces, weighing 42 troyounces and 451 grains of a spirit of nitrous ether, which had a s.g. at 4°C. or 39.2°F. of .8308. At 15.6°C. or 60°F. .8217. At 25°C. or 77°F. .8148. When 3 c.c. (=2.465 grams.) of this freshly made spirit was tested by the nitrometer it gave 35 c.c. of liberated gas, thus indicating (35÷6.66=) 5.25 p.c. of ethyl nitrite.

If the 216 grains of ethers in the end flask be added to the 3 troyounces and 277 grains, then this spirit will contain 8.33 p.c. of the complex ethereal product of the distillation, and 5.25 p. c. of this will be ethyl nitrite, and 3.08 p.c. will be other ethereal products.

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*This is not the entire product of an operation, because in these experimental trials, wherein the specific gravities were taken, there was always a considerable loss of ether. The average of the 5 distillations is 3 troyounces and 373 grains, to which the average 216 grains from the final flask when added makes an average product of 4 troyounces and 109 grains. This diluted with 11 times its weight of alcohol gives 24348 grains, or 50 troyounces and 348 grains as the average finished product.

This finished spirit of nitrous ether was neutral to neutral litmus paper, but required 2 c.c. of stronger water of ammonia (officinal 28 p.c.) to cause it to turn neutral litmus paper blue. Long experience has taught the writer that this small addition of ammonia is important to the keeping properties of the spirit, while therapeutically there can be no objection to it. The ammonia deepens the yellow tint of the spirit very much, probably by converting the traces of aldehyd into aldehyd resin, because after this the potassa test does not deepen the color in 24 hours.

The proceeding which is perhaps of greatest importance to all processes which obtain these ethers by distillation is the use of ice in condensing the vapors. Many of the details here given show how difficult it is to condense all the ethers, and how difficult to prevent a rapid loss, even on very moderate exposure, after they are condensed. The Pharmacopœia of 1880 is the first to direct the use of ice, thus improving on the Br. P. of 1867, which simply directs the receiving flask to be kept cool with iced-water if necessary. But in no pharmacopœia up to this time has the copious use of ice been properly emphasized or insisted on as it should be, for the writer is well assured that the difference in the yield of condensed ethers between processes conducted with and without ice, will often reach the proportion of one-half. And, between the partial use of ice, and the copious use of ice and iced-water the difference will often be 10 to 20 p.c. In this improved process as here given iced-water was continuously dropped upon the beak of the retort, and the globular, tubulated receiver, and final flask were both imbedded in finely crushed ice; but the supply of water for the Liebig's condenser was not iced, but was not lower than 20°C. or 68°F., and this of course condensed very little of an ether whose boiling point is said to be 18°C. or 64.4°F. If this condenser had been supplied with iced-water the results would have been considerably higher. That is, the finished spirit would have been no stronger, but there would have been more of it, since it is the washing and diluting steps of the process which so well control the strength.

CHANGES BY EXPOSURE AND KEEPING.

The U. S. P. very properly directs that this preparation should be at once put into small glass-stoppered bottles, and be kept in a cool dark place. Bottles of 120 c.c. or four fluidounces capacity are as large as should ever be used for storing spirit of nitrous ether, because in dispensing it for use, the physician or pharmacist rarely wants more than this quantity at any one time, or perhaps within a day or two of any given time, and in this way only could have it always in good strength and condition. But any manufacturer who would sell it only in four ounce g.s. bottles, at a proper price for the spirit and bottle, would simply sell very little of it,—far too little to keep his stock fairly fresh when it went out. It is for this reason mainly that this preparation should never be bought by the pharmacist, but should always be made by him, in never over the quantity, but generally in half the quantity, of this improved process. If made on the large scale and put up in one and three and a half pound bottles, to meet the general demand of the pharmacist, the best that can be done by the manufacturer is to put it up of over-strength, so that if fairly well managed after leaving his hands, it will not be very much under-strength when it goes into use. A portion of about 500 lbs. was adjusted by nitrometer to a strength of 5.4 p.c. of ethyl nitrite. After being put up in an assortment of sizes of 3½ lbs., 1 lb., ½ lb. and ¼ lb., a bottle taken and tested gave only 5.08 p.c., when it was expected to have been,—as it should have been,—at least 5.2 p.c. But this was in warm weather, when the loss would be at its maximum rate. The writer has always believed that the cause of greatest loss in strength in well made spirit of nitrous ether, from strong alcohol, is not molecular change, but evaporation. The very low boiling point of the constituent ethers, and the remarkable rapidity of their atmospheric diffusion, leads any one who handles them much, to know how difficult they are to condense, and to keep in a liquid state, and how very rapidly they leave the alcohol with which they are diluted. To throw some new light upon this important part of the subject, the following table was constructed.

TABLE No. 2.—SPONTANEOUS EVAPORATIONS.

On a day when the room temperature did not vary .3° from 20°C. or 68°F. from early morning till late at night, 3 low, wide, Griffin beakers of about 300 c.c. capacity and similar weight, and diameter, for surface area, were selected for the spontaneous evaporations. Into one of these was put 100 c.c. =80.50 grams. of alcohol, s.g. .8148 at 15.6°C., from which the spirit of nitrous ether had been made. Into each of the others was put 100 c.c. =81.24 grams. of spirit of nitrous ether of s.g. .8214 at 15.6° C., which gave a nitrometer indication of 5.050 p.c. of ethyl nitrite. These beakers were placed a few inches apart near the centre of a work table in the middle of the room, so as to be similarly affected by the room currents of air. The one with alcohol, and one of those with the spirit, were weighed every hour for 12 consecutive hours,—then again after 11 hours interval, and finally for 3 consecutive hours. The duplicate beaker with the spirit, was tested by nitrometer every hour for the 12 hours, although it failed to give any indication of ethyl nitrite after the 10th hour.

The losses by spontaneous evaporation at 20°C. are given in percentage by weight for the alcohol and the spirit, and also by percentage by nitrometer indication for the spirit,—no temperature nor pressure corrections.

Successive hours.	ALCOHOL. Loss on 80.50 grams			Spirit of Nitrous Ether. Loss on 81.24 grams			Spirit of Nitrous Ether. Loss of Strength by Nitrometer.			Difference in percentage rate of loss in weight of the Alcohol and Spirit.		
	Actual loss.	Percentage loss.	Percentage difference per hour.	Actual loss.	Percentage loss.	Percentage difference per hour.	Percentage indication per hour.	Percentage Cumulative loss per hour.	Percentage difference per hour.	Alcohol.	Spirit.	Difference.
	on 80.50	on 80.50		on 81.24	on 81.24		5.050	5.050				
1st..	.32	.40		1.23	1.51		3.212	1.838	1.838	.40	1.51	1.11
2d ..	.68	.84	.44	2.20	2.71	1.20	2.012	3.038	1.200	.84	2.71	1.87
3d ..	.98	1.22	.38	3.05	3.75	1.04	1.441	3.609	.571	1.22	3.75	2.53
4th .	1.31	1.63	.41	3.71	4.57	.82	1.207	3.843	.234	1.63	4.57	2.94
5th .	1.62	2.00	.37	4 34	5.34	.77	.685	4.365	.522	2.00	5.34	3.34
6th .	1 91	2.37	.37	4.88	6.01	.67	.360	4.690	.325	2.37	6.01	3.64
7th .	2.12	2.63	.26	5.36	6.60	.59	.288	4.762	.072	2.63	6.60	3.97
8th .	2.51	3.12	.49	5.79	7.13	.53	.135	4.915	.153	3.12	7.13	4.01
9th .	2.81	3.49	.37	6.16	7.58	.45	.054	4.996	.081	3.49	7.58	4.09
10th	3.13	3.89	.40	6.52	8 08	.45	.027	5.023	.027	3.89	8.08	4.14
11th	3.43	4.26	.37	6.86	8.44	.41	trace.	5.050		4.26	8.44	4.18
12th	3.71	4.61	.35	7.19	8.85	.41	none.			4.61	4.85	4.24
Farther loss :												
in 11 hours	3.52			3.75								
Per hour for 3 hours	.24			.27								

This table shows that under given known conditions alcohol of 93 p.c. evaporated spontaneously at a fairly uniform rate during 12 hours, and lost in that time 4.61 p.c. of its weight :—that a spirit made from this alcohol, under the same conditions, lost nearly three times as much in the first hour, and then diminished the rate of loss, rapidly at first and more slowly afterward, until in 12 hours it had lost 8.85 p.c. of its weight,—had lost every trace of ethyl nitrite, and had its rate of loss reduced almost to the rate of the alcohol.

The 3d and 11th columns of this table show the percentage cumulative rate at which the alcohol evaporated.

The 6th and 12th columns show the percentage cumulative rate at which the alcohol and ethers evaporated when mixed as spirit of nitrous ether.

When the alcohol rate is subtracted from the spirit rate, as in the 13th column, the difference gives an approximate idea of the rate at which the ethers were lost independent of the alcohol.

Then as there was 5.05 p.c. of ethyl nitrite in these ethers, and as 4.24 p.c. of this was accounted for by the nitrometer, before it disappeared altogether from the spirit, it follows that not more than .81 p.c. at most, could have been decomposed so as to take it out of the reach of the nitrometer during the 12 hours of exposure to air and light in an open vessel of broad surface.

The continued difference, in the rate of evaporation, between the alcohol and the spirit as shown in the last line of the table, after 26 hours' exposure, indicates that the ethers do not go off together, but that some of them are left in the spirit long after all the nitrites are gone; for if the ethers were all gone, the alcohol left, in both cases, should evaporate at the same rate. The odor and taste of the remaining spirit also indicate the presence of characteristic ethers, because it has the strong odor and taste of good spirit of nitrous ether.

It seems only necessary to glance at the very rapid rate of loss in the third division of this table to realize how much care and skill are required in making, keeping and dispensing, in order to have it of proper quality.

This very rapid rate of loss by diffusion was then illustrated in another way. A one pound bottle of spirit which had been made just one month, was brought from the cellar, and was found to give a nitrometer indication of 5.1 p.c. ethyl nitrite. Prescription quantities were taken from this bottle, during hot summer weather, —sometimes daily, sometimes two or three times a day, and sometimes not for one or two days. Throughout the 23 days of the experiment the bottle was opened over 40 times, and at the end the spirit remaining did not exceed two fluidounces. The portions poured out were every few days tested by nitrometer, nine testings having been made in the 23 days. During the first week about one-third of the bottle was used and the indication had then fallen to 4.9 p.c. During the second week it fell to 4.4 p.c. During the third period of 9 days it fell to 3.5 p.c. The last of the spirit was slightly acid to litmus paper when held beneath the surface, but did not effervesce with bicarbonate. Had this quantity of spirit been dispensed from four ounce vials the loss in strength would have been insignificant. This experiment was confirmed by a partial repetition under varying conditions, and the conclusion reached by means of the table, and these experiments is, that well made spirit from 93 p.c. alcohol loses its strength mainly by evaporation or diffusion, and only to a slight extent by decomposition, even with a practical degree of air contact. And farther, that by good ordinary management from a succession of four ounce bottles, it may always be dispensed within two or three-tenths per cent. of its orginal strength as made.

The actual loss by keeping or storing in ground stoppered bottles, will now be shown by another table. Here the loss by diffusion or evaporation is very slight, the bottles having been opened a very few times between the testings. But as no stoppers, however well ground, are tight against vapors under pressure, though perfectly tight to liquids, the loss by diffusion is not insignificant when long periods of time, such as one or more years is embraced in the experiment.

TABLE No. 3.

Showing approximately the change which occurs in keeping Solutions of Ethyl Nitrite, and Spirit of Nitrous Ether, of various alcoholic strengths, the losses embracing both vapor leakage and chemical change. Many of the specimens were tested twice,—and a few three times, the losses being always greater in proportion to the number of times the bottles were opened :

Specimen Number.	DESCRIPTION.	ALCOHOL. Strength of Alcohol used in Making.		S.G. of the Solution or Spirit at 15.6°C. or 60°F.	ETHYL NITRITE.			
		S.G. at 15.6°C.	Per cent. of water present.		Original proportion when made. Per cent.	Age of preparation at final testing.	Strength at final testing. Per cent.	Percentage. Loss per month.
1.	5 per cent. Solutions of pure Ethyl Nitrite in alcohol of various strengths.	.7938	.01	.7984	5.196	5 months	5.000	.000
2.		.7943	.16	.7995	5.000	"	5.000	.000
3.		.8141	6.90	.8185	5.000	"	4.984	.003
4.		.8145	7.00	.8184	5.000	"	4.857	.029
5.		.8191	8.70	.8234	5.000	"	4.696	.061
6.		.8390	16.30	.8419	5.000	"	3.265	.347
7.		.8616	25.60	.8635	5.000	"	3.090	.382
	SPIRIT OF NITROUS ETHER.							
8.	Made Oct. 11, 1886.	.8140	6.90	.832	3.000	30 mo's.	1.819	.039
9.	" Jan. 28, 1887.	.8142	6.90	.832	3.000	27 "	2.225	.029
10.	" " 11, 1888.	.8138	6.75	.832	3.000	15 "	2.468	.035
11.	" " 8, 1889.	.8143	6.90	.825	3.000	5 "	2.720	.056
12.	" May 21, 1889, U. S. P., 1860..	.8180	8.33	.837	5.742	1 "	4.681	1.061
13.	" May 21, 1889, U. S. P., 1870..	.8180	8.33	.824	1.727	1 "	1.545	.182
14.	" Feb. 4, 1889, U. S. P., 1880..	.8204	9.00	.824	2.828	4 "	2.454	.094
15.	" April 4, 1889, Improved	.8148	6.90	.822	5.255	3 "	4.803	.151
16.	" April 20, 1889, Br., with stronger alcohol..........	.8148	6.90	.828	5.454	2 "	5.430	.012

The above table is approximative only, as no corrections for pressure or temperature were made in using the nitrometer. And the first line of the table shows that, in one case at least, the error reached almost .2 p.c., since a solution of 5.196 p.c. appeared to have lost in 5 months .196 p.c., when in reality it had lost nothing. In the last line also, a temperature error in the opposite direction makes the loss appear less than it really was. But taken as a whole, the showing of the table is undoubtedly trustworthy, and the main points are that there is little or no practical difference in the keeping, between solutions of pure ethyl nitrite and spirit of nitrous ether, since preparations containing the same amount of water (see for example Nos. 4 and 9), changed at about the same monthly rate. Next, that the presence of water in the alcohol of dilution is probably the sole cause of chemical change, the remainder of the loss being by diffusion or evaporation. And, finally, that when the alcohol of dilution is not less than 93 p.c., and when the stoppering is good, the loss in keeping is insignificant, and that liability to chemical change is not a serious objection to spirit of nitrous ether. This being the case there is no good ground for the British proposal to substitute for it the alcoholic solution of pure ethyl nitrite.

There are, however, serious difficulties in the way of using spirit of nitrous ether which are to be mentioned under the therapeutic considerations; and it will be there shown that these difficulties are of the same kind, and no less in degree when alcoholic solutions of pure ethyl nitrite are substituted.

The specific gravities of the table although given at 15.6°C. only, were also all taken at 4°C. and are compared with the same volumes of water at the same temperatures. The difference of s.g. between the two temperatures is practically .0090, so that when the s.g. at 4°C. is required it is obtained by adding .0090 to the s.g. at 15.6°C.

The decomposition which produces acidity in spirit of nitrous ether by keeping, does not occur in well-made spirit, from strong alcohol, so long as it is unopened and well stoppered. This decomposition appears to be of a different kind, and to be due mainly to exposure to light and to atmospheric oxidation. It occurs in solutions of pure ethyl nitrite, but not to the same degree from the same exposure; and the change is more rapid, as the alcohol of dilution is weaker in both cases.

TESTS.

Although Mr. Allen's method of testing spirit of nitrous ether by nitrometer is not entirely trustworthy, but as he himself points out, —*Pharm. Journ. and Trans.*, Sept. 25, 1886, p. 256,—“ merely a ready method of ascertaining with considerable approach to accuracy, the strength of such preparations,”—it is still so much the easiest method that has yet been proposed, and so useful, that until practical pharmacy progresses much beyond its present condition, it really leaves little to be desired. Then, if during the time when the nitrometer proper may not be found in general pharmacy, some still less trustworthy application of the same method, such as that proposed and figured in this paper,—be admitted to use,—very much will be gained in the testing of spirit of nitrous ether, because in the presence of this method the other tests are of but little importance.

Color, odor and taste amonnt to very little, even in description. If a small amount of ammonia be added, as is here strongly advised, upon the results of a long experience, the spirit will be rather distinctly yellow in color from the production of aldehyd resin. And the odor and taste will vary perceptibly in proportion as the basis of the spirit is more or less pure ethyl nitrite, since pure ethyl nitrite does not give quite the odor and taste of spirit of nitrous ether.

If the writer's conclusions, in regard to the prime necessity for very strong alcohol in this preparation be admitted, then specific gravity becomes an important test,—but not as formerly when high specific gravity was taken as an indication of a large quantity of the ethereal basis. Now, it is important that the s.g. be as low as possible to indicate the high strength of alcohol used in making. A spirit that is well made from alcohol having a s.g. of .8148 at 15.6°C. will contain about 8 p.c. of the complex ethereal liquid, 5 p.c. of which will be ethyl nitrite, and such a spirit will have a s.g. of .822 at 15.6°C. Then .822 less .8148 is equal to .0074 difference. This difference subtracted from the s.g. of any spirit which gives a nitrometer indication of 5 p.c. ethyl nitrite, will give about the strength of the alcohol that has been used in making the spirit. Good spirit of nitrous ether will have a s.g. not above .825 at 15.6°C.

When made from strong alcohol it has very little tendency to become strongly acid by any necessary or even careless exposure. A one-pound bottle mentioned elsewhere as having been dispensed with frequent opening and exposure, was at the end but slightly, and not hurtfully, acid. There is no therapeutic objection to slight acidity; and it is even probable that any degree of acidity capable of occurring, in any ordinary management, of a well made spirit, is rather a therapeutic advantage in this, as in any, febrifuge. The test for acidity by either bicarbonate of sodium or bicarbonate of potassium is of very little value, because neither salt is soluble in a spirit made from strong alcohol, and there is very little effervescence with either from spirit pretty strongly acid. Litmus paper is a much better, and a sufficient test, though it gives little information as to the degree of acidity. The degree of acidity is certainly not hurtful when 5 c.c. of the spirit, with two or three drops of solution of phenolphthalein is rendered pink by not over 1.5 c.c. of volumetric solution of soda.

The boiling test at 63°C. proposed by this writer 30 odd years ago, and in the U. S. P. since 1860, is of no value, because even the worst samples have some ethers, and these are freed, to a certain extent, by this test.

All well made spirit has traces of aldehyd, and poor spirit or badly made spirit is not likely to have more, but actually has less than that which is good. No spirit seen by the writer in all his experience has been quite free from aldehyd, and none has had more than unimportant traces of it. The test for aldehyd by dilute solution of potassa is a good one, but the poorer commercial spirits stand this test better than the good ones, because the proportion of aldehyd increases with the proportion of the ethers. If a 5 p.c. spirit be diluted with alcohol to a 1 p.c. spirit, the latter will stand the aldehyd color test five times better than the former. A good 5 p.c. spirit diluted with an equal volume of about 4 p.c. solution of potassa, will become of a full yellow color in about 6 or 8 hours, and will not become sensibly deeper in 24 hours. A 5 p.c. solution of ethyl nitrite treated in the same way only becomes of a pale yellow. The proportion of aldehyd roughly indicated by this test is at best very small, and so far as any known effect of aldehyd on the human economy is concerned, must be unimportant. It has, however, always been present in spirit of nitrous ether, and is therefore a component part.

The ferrous sulphate test of the British Pharmacopœia and the ferrous chloride test of the German, appear both intended to show the presence of ethyl nitrite, and they are useless, because they are no more characteristic than the sensible properties.

Any spirit of nitrous ether, or solution of ethyl nitrite which contains a proportion of ethyl nitrite greater than .25 p.c., when shaken for a moment with twice its volume of water and then allowed to stand, will give a fine effervescence of gas which slowly rises to the surface of the liquid. The bubbles of air shaken into the liquid, being comparatively large, rise quickly to the surface, but the effervescence of decomposition consists of very fine bubbles, which continue to separate for a minute or two, and rise more slowly to the surface. The quantity of this effervescence is proportionate to the amount of ethyl nitrite present.

The single quantitative test, by potassium permanganate, of the U. S. P. must have been adopted on purely theoretical grounds, upon the recommendation of some one who had never tried it. It depends upon the conversion of the total ethyl nitrite into potassium nitrite, and then determining the amount of the nitrous acid present by the amount of permanganate required to oxidize the nitrous to nitric acid. This is of course correct in principle, but from surrounding conditions is quite impracticable. Even if the conditions were favorable, the time required is too long to fit the process for testing. After macerating with potassa for 12 hours, the solution is diluted with water, and must stand in an uncovered beaker until the odor of alcohol has disappeared, for if any alcohol be left it will decompose permanganate just as nitrites do. In a critical trial of this test, 4 days standing, in warm weather, was required to lose the odor of alcohol, and yet alcohol must have been present, and so another day was given. Then two testings, carried on side by side, required different amounts of permanganate, but both very much more than the prescribed quantity, and both continued to decompose fresh additions of permanganate made from time to time for 24 hours after the excess had been used. A third trial under better conditions than those of the U. S. P. again gave results far too high. The quantity given by the U. S. P. is calculated correctly for about 4 p.c. of ethyl nitrite, but other matters are present which belong there, and which decompose permanganate.

THERAPEUTIC CONSIDERATIONS.

The writer has never been able to assent to the proposition that ethyl nitrite is the only element of therapeutic value in spirit of nitrous ether, and therefore that a solution of this ether in alcohol should take the place of the solution of the complex ethereal liquid, in medicine. This view, taken through many years past, has been of late strongly advocated on the high authority of the Phamaceutical Society of Great Britian, and has been ably discussed in some of its principal branches. The drift of this discussion is well shown in a paper entitled "Comparative Effects of Spiritus Ætheris Nitrosi and Solution of Nitrite of Ethyl, by D. J. Leech, M. D., F. R. C. P., Professor of Materia Medica and Therapeutics in the

Owens College, Manchester." This paper is published in *The Pharm. Journal and Transactions* of London, No. 965, December 22d, 1888, page 490.

Before this ground can be safely or wisely taken a far more extended and thorough investigation should be made;—because, first, the favorable experience of some 600 years (from Raymond Lully in the 13th century), with preparations which, for a long time, were crudely made and badly kept, should not be so easily set aside. These have often contained but little ethyl nitrite, but always a considerable proportion of other ethereal products, and the sensible properties have been fairly uniform.

Second,—because, under the most favorable conditions, ethyl nitrite does not constitute over three-fifths of the complex ethereal product which is the basis of spirit of nitrous ether, while the other two-fifths belong to an ethereal series known to have definite physiological effects.

Third,—because a solution of ethyl nitrite keeps no better than well made spirit of nitrous ether, when both are made from alcohol of the same strength; whilst, when in actual use, and diluted with water, the decomposition is scarcely less rapid, and leaves a residue much poorer in ethereal products. The results of the decomposition by water are probably, though not certainly, the same in both solutions, and the ethyl nitrite in both is probably the element which splits up; but, the nature of the products of this decomposition, and what becomes of them, has not been shown.

The effects of spirit of nitrous ether as a febrifuge, a diaphoretic and diuretic, are too long and too well established to be called in question here. It reduces arterial tension so promptly that there are few agents in the materia medica that so quickly relax the entire circulation, and thus so promptly relieve cardiac and pulmonary distress. This relaxation and relief is easily seen to extend to the skin, mucous membranes and kidneys, and therefore must affect all the organs, and as a general result the temperature falls, and defervescence is greatly favored. As alcohol and water, although not without effect, do not give these results, it follows that the other elements of the spirit are, in combination with the alcohol and water, the active agents.

A common prescription by which such effects are obtained, is one fluidounce each of spirit of nitrous ether and water,—a teaspoonful in a tablespoonful of water being given every one, two or three hours. Given every hour, as a febrifuge, such a prescription would last 16 hours. Or, as more commonly given, every hour for eight hours and then every two hours, it would be taken in 24 hours,—or with a night interval, in 36 to 48 hours, so that this is about the longest time such a prescription would be kept. Such a prescription made from a spirit of nitrous ether indicating 5 p.c. develops 4° or 5°C. rise of temperature. A fine effervescence at once occurs throughout the mixture, and soon exerts much pressure upon the cork of the vial. Such an effervescence occurs on mixing strong alcohol and water, but not to the same degree. The gas thus liberated is colorless,—has only the odor of the spirit, and does not develop orange fumes when it comes in contact with the air, as nitric oxide, or NO, should do. About five-sixths of this gas is absorbed by shaking with cold solution of ferrous sulphate, yielding a nearly black solution. After the first effervescence of this gas is over, no farther pressure within the vial is noticeable in the many openings throughout the 48 hours, and the sensible properties of the liquid from first to last are apparently the same. Tested by the nitrometer when freshly made, at the end of the effervescence, the indication, for the spirit used, is found to be reduced to 3.3 p.c.,—1.7 p.c. having disappeared, so far as the nitrometer indication is concerned. Assayed again in 24 hours, the indication was 2.2 p.c. and in 48 hours 1.3 p.c., and the mixture was then acid to litmus paper. It is thus shown that a prescription of this kind will, in actual use, lose in 48 hours 3.7 p.c. of its nitrometer indication, or 74 p.c. of its ethyl nitrite, but it has not been proved that the loss in therapeutic value is as great.

It is just here, however, that the great difficulty and uncertainty in the use of this agent occurs. It has been abundantly shown that when well made and of good quality, it is not very difficult to keep, for any reasonable time, in a condition entirely fit for use at any moment. And that if, in recognition of its true nature, it be kept in small well stopped bottles, it can always be dispensed for use in the same good condition. But as soon as it is mixed with water, rapid decomposition ensues. Occasionally it is prescribed undiluted, to be given in 30 minims to a teaspoonful added to half a wineglassful of water at the time of taking. But much more frequently it is ordered simply diluted with water, or in mixtures of which water is the base, and then in 5 minutes or before it leaves the hands of the pharmacist it will have lost about 34 p.c. of its ethyl nitrite, so far as the nitrometer indication is to be trusted. If this very great loss can be prevented, or be brought within moderate limits, the agent may be saved. But modern medicine will not long tolerate a remedy that in use deteriorates at the rate of about 33 p.c. every 24 hours.

The late Mr. John Williams, F.I.C., F.C.S., of London, in a paper entitled "Note on the Preservation of Ethyl Nitrite," read before the British Pharmaceutical Conference of 1886, see *The Pharm. Journ. and Trans.* for Sept. 25th, 1886, page 255, proposed as a preservative of ethyl nitrite, a solution of one part glycerin and two parts absolute alcohol. But in the writer's hands this did not prove more satisfactory than absolute alcohol alone, as the latter left little to be desired, and Mr. Williams did not propose to apply glycerin to spirit of nitrous ether. Taking his idea, however, the writer applied it to the preservation of spirit of nitrous ether during the few days when it was diluted for use, and found it to be fairly successful. That is, the decomposition was very much diminished and retarded, so that prescriptions being made up from a good 5 p.c. spirit with about 25 p.c. of glycerin, might be effectively used for 48 hours. Numerous experiments with glycerin and water in different proportions as a vehicle for solution of pure ethyl nitrite and for spirit of nitrous ether, led to a trial of simple syrup for the same purpose, and this proved to be better than glycerin. The following table gives the result of these trials:

TABLE No. 4.

Showing the Comparative Results of the use of water, and mixtures of glycerin and syrup, as vehicles for solution of Ethyl Nitrite, and Spirit of Nitrous Ether, in prescriptions. Prescriptions were made up of equal measures of the different vehicles with 5 p.c. solution of pure Ethyl Nitrite in nearly absolute Alcohol;—and of 5 p.c. Spirit of Nitrous Ether in 93 p.c. Alcohol;—and these mixtures were tested by nitrometer when freshly made, and then every 24 hours during their continuous use. The results are stated in percentage of Ethyl Nitrite remaining of the original 5 p.c. in the solution and spirit, at the times of testing by nitrometer. When the vehicle is a mixture of Glycerin and Water, or of Syrup and Water, these are in equal measures.

TABLE NO. 4.

Equal Measures of Pure Ethyl Nitrite, or of Spirit of Nitrous Ether, With Various Vehicles for Prescription Use in Administration.	Original Strength in Ethyl Nitrite.	Nicrometer Indication.					
		When Freshly Made.	After 24 Hours.	After 48 Hours.	After 72 Hours.	After 96 Hours.	After 120 Hours.
		P. C.	P. C.	P. C.	P. C.	P. C.	P. C.
Ethyl Nitrite Solution with Water	5 p.c.	2.88	1.44	.70	....	....	....
" " " " Glyc'n and W.	5 p.c.	3.80	3.21	2.00	....	....	....
" " " " " "	5 p.c.	3.66	2.52	1.50	....	....	....
Spirit of Nitrous Ether with Water	5 p.c.	3.00	1.77	1.30	.83	.66	.35
" " " "	5 p.c.	3.30	2.20	1.30	....	....	....
" " " Glyc'n and W.	5 p.c.	4.20	3.15	2.57	2.06	1.65	1.31
" " " " "	5 p.c.	4.32	4.20	3.40	2.61	1.41	....
" " " Simple Syrup.	5 p.c.	4.20	3.89	3.54	3.36	3.15	2.55
" " " Syrup and W.	5 p.c.	4.18	3.95	3.42	3.30	3.00	2.40

These trials show conclusively that in dispensing spirit of nitrous ether for bedside administration, if it be diluted with an equal measure of simple syrup, it can be very effectively used for three or four days, even in summer, for these trials were made in very warm weather. As two to three days is the common limit of the use of this agent, and as it is now recognized that all prescriptions should be directed in small quantities, and be frequently renewed if required, this management will bring this agent into a new sphere of useful activity. The simple proceeding of carefully buying and keeping the spirit in small bottles so that it shall lose little, and then of diluting it with syrup for use, is within the reach of all physicians and pharmacists who choose to avail themselves of it, and its importance is easily recognized when it is seen what becomes of the spirit when diluted with water.

The slight degree of acidity which is acquired by good spirit of nitrous ether in keeping is from the formation of traces of acetic and nitric acid, and these by reacting with strong alcohol yield the corresponding ethers. But neither these acids nor their ethers are therapeutically objectionable in the spirit, but on the contrary are remedial in the same direction as the spirit itself. In compound prescriptions into which agents decomposable by acids enter, the acid is objectionable, but in such cases it is very easily neutralized by a few drops of ammonia, and the traces of ammonium salts thus formed are in no known instance at all objectionable. The habit of many pharmacists and physicians of keeping a crystal or two of potassium bicarbonate in each bottle of spirit after it is opened for use, is an excellent one, and it avoids all acidity, but it has, of course, no effect in retarding the loss by diffusion,—that is, the disproportionate evaporation of the ethers off from the alcohol.

COMMERCIAL SPIRIT OF NITROUS ETHER.

In the writer's paper of 1856, republished here, an account is given of the spirit of nitrous ether of the common market, as judged by a process of fractional distillation. The nitrometer was not then in use, nor was there any easy way of approximating the proportion of ethyl nitrite present. The fractional distillation gave a fair account of the total complex ethers present, but it is now known that the proportion of ethyl nitrite that these contained was variable, and not generally over one-half to five-eighths. Hence the estimated percentage of dry ethers then obtained from the commercial articles was very much above the percentage of ethyl nitrite. Yet in all the light of more recent experience and investigation, it seems probable that the average of the commercial spirit in ethyl nitrite was then above 1 p.c.

Now again, February, 1889, after an interval of over 33 years, the writer went into the market and got original one-pound bottles of the products of all the makers that were known to the wholesale houses. Of these makers there were seven, and the average wholesale price per pound, for spirit and bottle, was about 48 cents. Five of the seven were obtained when asked, and therefore represented what was present in the market, ready to supply orders, but the remaining two were not delivered for two weeks or more, and as no secret was made as to their being wanted by the writer as samples for examination, there is room for a suspicion that they might have been specially prepared. Both were said to be made by diluting ethyl nitrite or "concentrated nitrous ether,"—one by the U. S. P. of 1870, the other by the U. S. P. of 1880. Every bottle of the whole seven bore the maker's name and label and claimed to be of "U. S. P." strength and quality. All were in cork-stopped bottles, and a few of the corks were so shrunken as to be so loose that they could be taken out with the fingers. All were loose enough to have admitted of escape of vapor, and there was no noticeable pressure within the bottles on opening. The three principal makers of 1856 have continued to make since that date, and their products are represented in both tables. Each bottle was tested by nitrometer as soon as opened,—was then corked again with the original cork. After an interval of two months they were again tested, and a third time after a second interval, but the first and third testings only are given in the table.

TABLE No. 5.

Commercial Spirit of Nitrous Ether of all the known makers whose products supply the New York Drug market in February, 1889. Tested for Ethyl Nitrite by the Nitrometer.

No. of Samples.	Description.	Specific Gravity at 15.6°C.	Approximate Strength of Alcohol used in making.	Nitrometer Indication.			
				Per cent. of Ethyl Nitrate when freshly opened.	Interval between Testings.	Per cent. of Ethyl Nitrite at Final Testing.	Per cent. of Loss per Month.
1.	Sample made by Improved Process of this paper...............	.822	93 p.c.	5.255	3 mo.	4.803	.151
2.	Sample made by Process of U. S. P. of 1880	.824	91 "	2.828	4 "	2.459	.092
3.	One pound bottle labeled Spt. Nit. Eth. U. S. P.	.846	81 "	.540	4 "	.426	.029
4.	One pound bottle labeled Spt. Nit. Eth. U. S. P.............. ...	.844	82 "	.923	4 "	.698	.058
5.	One pound bottle labeled Spt. Nit. Eth. U. S. P................	.845	81 "	.824	4 "	.495	.082
6.	One pound bottle labeled Spt. Nit. Eth. U. S. P...............	.836	85 "	.504	4 "	.441	.016
7.	One pound bottle labeled Spt. Nit. Eth. U. S. P............. ...	.841	82 "	.680	4 "	.594	.022
8.	One pound bottle labeled Spt. Nit. Eth. U. S. P. 1870..........	.846	81 "	2.594	4 "	2.270	.081
9.	One pound bottle labeled Spt. Nit. Eth. U. S. P. 1880	.825	91 "	2.567	4 "	2.486	.020

Samples Nos. 8 and 9 were not found in the market with the others, but were supplied to order a week or two later, with the message that they were made from "Concentrated Nitrous Ether." A pound bottle of this "Concentrated Nitrous Ether" of the market, made by the firm which first put it upon the market some years ago, was bought. On examination this was found to be nearly pure ethyl nitrite, and when, in accordance with the label, it was mixed with alcohol in the officinal proportion of one part to 19, it gave a solution which when tested by nitrometer gave an indication of 4.74 p.c. Had it been pure ethyl nitrite the indication would have been about 5.2 p.c. The solution in 3 months keeping was reduced to 2.280 p.c., equivalent to a loss of .821 p.c. per month, and its behavior was alogether very much like the solutions of pure ethyl nitrite. Like these it differed in sensible properties from all well-made spirit of nitrous ether,—or in other words it did not make the agent which for so long has been known as spirit of nitrous ether, yet gave a solution many times better than any other commercial article. This, therefore, in its relation to the market, must be classed with samples 8 and 9, and they represent the products of several makers of this "Concentrated Nitrous Ether" now on the market for a few years past. If the British proposition to substitute solution of pure ethyl nitrite for spirit of nitrous ether be wise and sound, then these preparations, so far as they have been used, have been quite in that direction for many years past. But the testimony of the few pharmacists whom the writer has met, who have tried this method of getting their supply of spirit of nitrous ether, has been that it does not yield a true spirit of nitrous ether (by sensible properties) and that it deteriorates very rapidly. It will be seen that this testimony agrees with the results of the writer. Until such solutions are supported by large and competent medical experience, and are then authorized by the Pharmacopœia, they are inadmissible. When admitted it will be time enough to discuss the disadvantages of managing a liquid whose boiling point is below the cellar temperature of most climates during one-third of the year.

The character of the spirit of nitrous ether of the market, as represented by samples 3 to 7 inclusive, is so very bad as to be, in the interests of medicine, disgraceful. Made from weak alcohol, by cheap processes, and put up in cork-stopped bottles, the 48c. per pound price, even, does not afford a large profit to the maker, and both price and quality are probably due to that kind of competition and overproduction in the common market through which the most important medicinal agents are judged and used by price alone.

It is not uncommon to hear a broker, who is going round the market pricing goods for his distant wholesale house, say, with his sarcastic smile, "Should think you would be afraid of killing somebody with your strong, high priced drugs."

Physicians appear to be losing one after another of their agents by joining in this pressure for price, and whether they, in the interests of their profession, can afford this they must be left to judge. Many of them have given up the use of spirit of nitrous ether entirely, and others seem to use it as a placebo, or as a vehicle, because it was handed down to them by their predecessors; and a reason for this is apparent when it is seen that commercial spirit of nitrous ether supplies perhaps not less than four-fifths of the total demand for the agent,—that 33 years ago the commercial spirit, on an average, contained, probably not much over 1 p.c. of ethyl nitrite,—and that now it contains not over .8 p.c. of ethyl nitrite, and that when mixed with water for administration nearly a fourth of this is lost before the first dose can be given.

It would be unjust to close this paper without an acknowledgment that much of the best work in it, and in other papers of this pamphlet, was not done by the writer, but was done by the younger eye and steadier hand of his assistant, Miss Mary L. Lovejoy. Her intelligent, careful work has made the undertakings possible, and if there be any credit, to her that much is due.

CASCARA.

The scarcity of the bark of Rhamnus Purshiana is now over (June, 1889), and plenty of bark of fair quality is to be had at moderate prices. Still, the best bark in the market now must have been collected too early to be in the best condition, and is of course quite unseasoned by age. During the scarcity the price for fair quality arose to 80c. per pound,—or to more than ten times the usual cost for good, well seasoned bark, and yet there was no time at which good bark could not have been bought if 85 or 90c. were offered. And bark steamed off, or chipped off, at improper seasons, was always present in the New York market, in abundance, at say 40 to 60c. per pound. Now, there are large amounts offered from Washington Territory and Oregon as well as from California at 18 to 20c., and there is much competition for September deliveries at about 10 to 12c. But now that there is plenty, there seems to be but little disposition to buy, and the probability seems to be that the old, glutted condition of the market is again to occur, with all kinds and qualities of bark, at prices too low to pay for collecting. During the scarcity, as large quantities of inferior bark were constantly being sold, it is pretty certain that these were used in the preparations, and it would be very interesting to know how these preparations upheld the character of the remedy.

Unusually large quantities of Buckthorn bark, Rhamnus frangula, were sold, at the same time, at low prices,—4 to 5c. per pound, —and the market gossip was that the barks were being largely mixed, and that preparations of Buckthorn were substituted under the fashionable name of "tasteless Cascara." Whether or not there was any truth in such reports, it is pretty certain that Buckthorn had better opportunies of extended use than ever before, and that when fairly used in competition with even the very best Cascara, it was found to be the better agent. Another such scarcity of Cascara would probably go far to demonstrate the general superiority of Buckthorn.

Among the prominent advantages of Buckthorn is the one that there can never be a scarcity of it, or any that is unseasoned, or of very poor quality, or of high cost, because, being a secondary product of powder making, it must always be present in large quantities, stripped only at the proper season, and at very low cost.

NEUTRAL OLEIC ACID.

The U.S.P. of 1880 describes its oleic acid as being "of a neutral reaction." The impossibility of an acid of neutral reaction did not occur to the Committee of Revision, and this writer at first fell into the same error, and described oleic acid as being neutral until November, 1883, when in these pamphlets, at page 400, he corrected the error by stating that it is never neutral to test paper. It, however, is still occasionally complained of, and returned, as being not neutral as the Pharmacopœia says it should be. Like many other errors, this one seems to require correcting over and over again, although should any other common acid be described as neutral in reaction, a mistake would be at once inferred.

MUSK.

Musk as a therapeutic agent has fallen into disuse, and the reason for its disuse, after once having had a fair reputation upon good authority, is open to inquiry. The few occasions when it is ordered among physicians' supplies in quantities from quarter of an ounce to one ounce, the order is generally countermanded promptly on mention of the price of a good quality. Like gold, it is an article the supply of which rarely exceeds the demand. The cost of pure musk is about one-half greater than pure gold, and its quality is by experts about as accurately determined as gold. It is used almost exclusively by perfumers, and its varieties are judged by the strength,—that is, the quantity,—and the quality of the odor. Musk which is entirely unadulterated, can be had at about $18.00 per ounce, but such has but about half the power of scenting that is possessed by $36.00 musk, and the quality of the scent may be inferior. The best pure musk of the market generally commands from $24.00 to $36.00 per ounce, and most of the lower grades are made from such by skilfull adulteration with dried blood or some other such vehicle. The two common grades are grain musk and pod musk, and although the latter is always supposed to be in the original pouch or pod of the skin of the musk deer, experts know better, and know that the two grades are equally liable to adulteration. Adulteration of musk, like all other adulterations, is practiced for profit, and hence a $36.00 musk adulterated with an equal weight of dried blood is not sold at half the price per ounce, plus the cost of the blood and the graining, but at as much more than this as the ignorance of the buyer will bear, and this will vary all the way from $20.00 up to $36.00, or the original cost of the pure musk.

Under this condition of market what becomes of the physician who wants to use musk in critical adynamic conditions wherein other agents have failed him, and wherein life hangs by a thread so slender that no reasonable chance, however slight, can be disregarded.

Perhaps he has musk bought from some of the price lists where he found it quoted from $6.00 to $8.00 per ounce and bought that of lowest price. Perhaps he has to send for it to the nearest town, and in both cases the chances are about ten to one that he loses his patient even if his case had been within the reach of pure musk to save. Losing his patient he determines to be forearmed for the next case,—say of adynamic diphtheria, in which Jacobi says pure musk is sometimes useful,—and sends to his druggist to get some. The druggist may send him word that pure musk will cost him $30.00 per ounce, in which case, in nine times out of ten, the order will be countermanded, because he will find musk quoted on many lists, that have been left with him by drummers, at less than one-third of that price, and the house which sells it at $9.00 may well make more money than that which offers it at $30.00.

TINCTURE OF CHLORIDE OF IRON.

The U. S. P. of 1870, in the pecuniary interest of pharmacy, but not at all in the interest of therapeutics, separated this preparation into two parts. It introduced an acid solution of ferric chloride under a faulty name, because the name gave no indication of its necessary excess of acid, and thus left the solution to be confounded with a normal solution of ferric chloride, which had long been in common use for an entirely different class of uses. Then, under the caption of Tincture of Chloride of Iron, it directed this acid solution to be mixed with a definite quantity of alcohol and to stand in a closely-covered vessel for at least three months. No other reason for separating the two steps of the old process into two preparations has ever been suggested than that of putting the iron solution into the hands of the large manufacturer, so that the pharmacist may buy it instead of making it, and thus get it at a lower cost and without any demands upon his own time or skill. No physician would ever have thought of this in his own or his patient's interests, and no physician of the Committee of Revision should have consented to it, because the result to the preparation could have been foreseen. Yet the Committee of 1880, after the result of ten years' experience had been realized, continued the plan. And to-day it is hard to find a specimen of the Tincture with any of the former ethereal odor or effect, and the Tincture has pretty much gone out of use for one important class of its former uses,—namely, as an antispasmodic and diuretic of a certain kind and quality in kidney and bladder affections. Indeed physicians of the present day know little of its uses in this class of disorders, simply because it has ceased to be useful, and, therefore, has ceased to be used.

The considerable excess of hydrochloric acid always used in the preparation was intended to slowly react upon the alcohol in the cold, so that by age much of this excess of acid, and a corresponding proportion of the alcohol would decompose each other with the formation of ethers that were to be effective in the preparation. Three months is not a sufficient length of time for this reaction, nor is six months sufficient. And beside this, the reaction does not occur so promptly nor so effectively when the elements are kept separately and only mixed three months before they are wanted. Then if these reactions do not occur as intended, the excess of acid present is much too great, and may affect the stomach primarily, and the whole organism secondarily, very unfavorably.

If the preparation is to be kept as it is, the excess of acid should be reduced at least one-half, and perhaps two-thirds, and then let the ethereal element go, since it is now no longer utilized. A little ether will, of course, be formed so long as there is any excess of acid, and probably, in three months, nearly as much would be formed from one-half as from the whole present excess of acid. Let any one who wants to demonstrate this for himself, titrate the free acid present in a freshly made officinal Tincture, and again at the end of the prescribed three months. He will find that it takes very careful, accurate work to find that any of the acid has been decomposed.

Why this mutual reaction between the acid and alcohol is so slow under the present pharmacopœial directions, and was more prompt under the old conditions is very difficult to know, but as an hypothesis it is not unreasonable to suppose that the reaction is started and hastened forward by the presence in the old way, of an unavoidable, small proportion of nitrous acid. Certain it is, that in all the Tincture of Chloride of Iron of the U. S. P. up to the revision of 1870, the ethereal odor had the element of ethyl nitrite present in it.

The officinal directions of 1860 are: "When effervescence has ceased, drop in Nitric Acid, constantly stirring, until it no longer produces effervescence. Lastly, when the liquid is cold add sufficient Distilled Water to make it measure a pint, and mix it with the Alcohol."

This yields a tincture which contains a little nitric acid, and all the nitrous acid the iron solution is capable of holding at a temperature near the boiling point, and such a tincture has, in six months or a year, a full ethereal odor in which ethyl nitrite is recognizable.

The present officinal directions are: "After effervescence ceases, apply heat, by means of a sand-bath, until the liquid is free from nitrous odor." This solution yields a tincture which in six months or a year has a mere trace of ethereal odor, without a suggestion of ethyl nitrite, and is very nearly as acid as when freshly made.

There is a pleasant mellowness and softness in the sensible properties of the 1860 tincture which are wanting in that of 1870 and 1880, and the writer is fully convinced that the first is the better therapeutic agent. In loyalty to the U.S.P. of 1870 he abandoned the 1860 process, but always made the tincture at once, and kept it for a year instead of three months, but ever since the difference between the tinctures was discovered by experience he has regretted having made the change, and desired to go back.

COMMERCIAL JALAP.

Since the note on Assay of Jalap in these pamphlets, a year ago, at page 1095, the markets of Hamburg, London, and New York have been carefully watched for samples of the drug which would, as aforetime, yield 12 to 17 p.c. of resin, and several lots of the best that could be selected have been bought and worked up into resin of jalap, but not a market sample has been found that yielded over 9 p.c., and only one lot which yielded over 7.5 p.c.

A special messenger going from a New York house to Jalapa in Mexico, was charged to get all he could that was produced in the old way in the old location, at any price. After a few months a shipment of less than 200 pounds was received from him, giving 16.9 p.c. of resin. This was, therefore, of the old kind and gave a good rich powdered jalap. In appearance and fracture, however, it was much inferior to many of the samples which under the same management gave 6.5 to 7.5 p.c. Farther search in the neighborhood of Jalapa and Perote has been successful in finding 400 to 500 pounds more, which is supposed to be now on the way from Vera Cruz, or waiting to be shipped with other merchandise. But if this messenger has obtained any explanation of the great deterioration in jalap from Mexico, he will be likely to keep it to himself for the commercial use of his principals.

THE PHARMACOPŒIA OF 1890.

The time appointed for the decennial revision of the Pharmacopœia is near, and the President of the Convention of 1880 has issued the decennial call upon the incorporated medical societies,—incorporated medical colleges,—incorporated colleges of pharmacy,—incorporated pharmaceutical societies,—the American Medical Association,—the American Pharmaceutical Association,—the Surgeon-General of the Army,—the Surgeon-General of the Navy, and the Surgeon-General of the Marine Hospital Service, to send delegates to form a Conveneion for the revision of the Pharmacopœia. These delegates are to meet in Convention in Washington on the first Wednesday of May, 1890.

Formerly the Conventions were made up exclusively from the medical profession, and only in 1850 was the important element of pharmacy present in these Conventions. From that time, as was foreseen, there was a very marked improvement in the work, and possibly, from the gain thus made, there seems to have been, of late years, a disposition on the part of the medical profession to take a less active interest in the work. The principal national organization, namely, The American Medical Association, has commonly treated the subject with indifference, but at one time decided very definitely that it would have nothing to do with it. In other medical organizations, if anybody wanted to be a delegate, he could easily get himself appointed, or if the subject was called up through the publication of the official notice, somebody would be appointed who did not want to go, or who might or might not go, and thus the matter has drifted along as though it was of small importance to the medical profession. On the other hand, the pharmaceutical profession, which has a more direct pecuniary interest in the subject, has continually increased in activity, discussing the subject in its organizations, and carefully selecting its very best men for delegates, and seeing to it that they accredited men who would be sure to go. Then if the best men in this profession were superior to the chance men of the medical profession, they would lead the Convention and the revision, of course, as should be the case, and whenever there was any contrariety of interests pharmacy would prevail. The true intrinsic interests of scientific medicine and pharmacy are, of course, absolutely the same, but the interests as they actually exist in practice, are not always the same. And, when they are not, those of medicine should always prevail, because their relation to the sick,—

the object of both,—is nearer and more direct. The pharmacist deals in medicines as a business,—the physician applies them as an art. Neither can ever do well without the other, but the one is much closer to the issues of life and death than the other, and cannot afford to trust these issues to a more distant dependence, which must always be more largely commercial or mercantile. Should the low, but not uncommon, standard of money be used to illustrate this relation, the position is, that the pharmacist makes his living off of medicines which he buys at one price and prepares and sells at another, while the physician makes his by applying these medicines to the relief of suffering. The Pharmacopœia is equally the reliance, the guide and the authority of both, but cannot wisely nor safely be entrusted to the control of either. There is no longer the least danger that pharmacy will not be fully represented in these Conventions, but the supineness of the medical profession to an interest so important is very much to be feared in its results.

The work of the last revision is understood to have been done almost entirely by sub-committees, and their work was collected, collated, corrected, arranged and re-written into uniformity of style and nomenclature, and was then put through the press almost entirely by Dr. Charles Rice, the Chairman of the Committee of Revision. This enormous labor, the character and quality of which very few have any adequate idea of, was quite unpaid, and money had to be borrowed to defray the actual outlay for expenses. Now there is plenty of money, and always will be in future if the book be fairly well managed, and therefore this taking of so much unpaid labor should never occur again, and ample provision should be made for trying every single process in the book, by competent hands, before it is finally adopted. Every article of material should be examined and every test be applied. The President of the Convention should be Chairman of the Committee of Revision, and he should be well paid, and be well supplied with money beside his pay. with which to employ competent aid for the work. All the work should be done under his immediate direction and control, and should then, as far as necessary, be submitted to sub-committees for repetition and confirmation, thus reversing the plan of the last Revision where there was no money with which to have the work done in this way. The Chairman of the last Committee of Revision, with his well-known scholarship, ability, energy and industry, and his now matured knowledge and experience in the work, is the man of all others fittest for President of this Convention of

1890, and for Chairman of the Committe of Revision if he can be induced to take the position. And the inducement most likely to have weight in influencing him to accept the position, would be to confer on him the entire responsibility, with the committee-men for his counsellors, and his sub-committees. This writer has worked enough for him and with him to know his peculiar fitness for this important work, and as he has been thoroughly tried in it during the past ten years, and has done all that was possible for one man to do, the writer is constrained to offer the opinion that the Convention will consult its best interests in trying every means in its power to get Dr. Rice to accept its presidency; and although neither a delegate nor a member of the Committee, the writer hereby, without fear of adverse criticism, nominates Dr. Rice for President of the Convention of 1890.

TESTING OF LITHIUM CARBONATE.

The U. S. Pharmacopœia is in error in its testing of lithium carbonate. The solubility is given as 1 part in 130 parts of water at 15°C. The British Pharmacopœia gives 1 part in 150, and Gmelin 1 part in 100. Prof. F. A. Fluckiger showed that it was soluble 1 part in 70, and less soluble in hot than in cold water, and this is doubtless the accurate proportion, but it takes much time and skill to make such a solution. One part in 80 to 85 of water, is, however, easily made, and is a very good practical test.

The Pharmacopœia requires that if a solution of the salt in diluted hydrochloric acid be evaporated to dryness, 1 part of the residue should be completely soluble in 3 parts of absolute alcohol. This test depends too much upon the presence or absence of water in the residue and in the alcohol to be of much practical utility.

The lithium chloride is a very deliquescent salt, and takes moisture from the air so rapidly that it is difficult to weigh it dry, and therefore it is difficult to get the 1 part so free from water that the water absorbed does not affect its solubility. Again, absolute alcohol attracts moisture in the same way, and after a very little exposure to air, has a corresponding amount of water. This water has also an effect upon its solvent power upon deliquescent salts. The absolute alcohol of the U. S. P. of the prescribed s.g. of .794 at 15.6°C. is not quite absolute, but contains about .075 p.c. of water. It is, however, as nearly absolute as is practicable,—or rather, is more nearly absolute than is practicable, for it is impracticable to find it in the markets lower than s.g. .7945, or .7946 at 15.6°C., and such alcohol contains between .1 and .2 p.c. of water.

With the salt quite dry, and weighed on a dry day, and with alcohol of .794 at 15.6°C. 1 part is not soluble in less than 6.4 parts of the alcohol.

With the salt fairly dry, and weighed with ordinary care, and with alcohol at about .7946 at 15.6°C. 1 part of the salt requires about 5.4 parts of the alcohol for complete solution at summer temperatures, say 27°C.

The "completely soluble" of the U. S. P. is, in an accurate sense, rarely or never realized, even in the best lithium carbonate obtainable in the markets. The solution is always cloudy, or slightly milky, but when filtered the residue is scarcely weighable on an ordinary balance, and is of no importance in medicine.

A test of the British Pharmacopœia whereby 1 part of the carbonate converted into sulphate, and ignited, yields 1.486 parts of anhydrous sulphate, is a very good test.

TINCTURE OF STROPHANTHUS.

Strophanthus seems to have so far sustained its earlier reputation as to come pretty largely into use as a cardiac stimulant which does not disturb the stomach as much as digitalis is liable to do. So much is it now used that it becomes quite important that the tincture should be of nearly the same strength everywhere. No less than six varieties of the seed are met with in commerce (Blondel), but only two of these are considered to be properly used; namely, S. hispidus, the brown seed, and S. Kombé, the greenish brown seed, the latter being generally preferred. The tincture, having originated in Scotland, upon the researches of Prof. Fraser, was, of course, made by British weights and measures, and as these are difficult to bring into accord with U. S. weights and measures, some confusion, and perhaps inaccuracy has existed. At first, for a short time, 2.5 avoirdupois ounces to a British pint of 20 (short) fluidounces were used, but at the suggestion of Mr. W. Martindale this proportion was changed, and the change was accepted by Prof. Fraser, to "1 part to 20 fluid parts." That is, one avoirdupois ounce to the British pint of 20 British fluidounces. But the British fluidounce is 437.5 grains of water at 60°F., while the U. S. fluidounce is 455.7 grains of water at 60°F.

To correct the British relation of 1 avoirdupois ounce to 20 British fluidounces,—or of weight to measure,—to the more accurate and convenient relation of the U. S. P. of weight to weight, it was necessary to know the s.g. of the British tincture, but this has been nowhere given. The British Rectified Spirit which is used as a menstruum for the tincture has the s.g. .838 at 60°F.

A tincture made by the British process, except that alcohol of s.g. .8914 at 60°F. was used, gave the s.g. .8931 for the tincture,—a difference between menstruum and tincture of s.g. .0017. This difference added to the s.g. of British Rectified Spirit would give the s.g. of the British tincture as .8397,—or say .840. This would make the 20 British fluidounces of British tincture weigh (as 1000: .840 ::8750:) 7350 grains, or 16 avoirdupois ounces and 350 grains, and this weight relation is 5 avoirdupois ounces of the powdered seed to make 84 avoirdupois ounces of tincture; or in U. S. P. expression it would be 5 parts of seed to 84 parts of tincture.

Seeds which have a dense, heavy or tough albumen are very difficult to exhaust, and that the exhaustion should be practically good, they must be finely powdered, or a menstruum must be used that will soften and disintegrate the albumen. That both these conditions may be reached to the greatest practical degree, the seeds after being well dried are powdered with half their weight of glass, in order to cut them up; and then the weakest, or most watery alcohol that will yield a clear tincture, is used for the exhaustion, so that the water may soften the albumen, and with the alcohol dissolve out the active principles. For these reasons a weaker alcohol than the British Rectified Spirit is desirable. This alcohol is just about 84 p.c., and a clear tincture can be made with alcohol of s.g. .8914 at 15.6°C., which is a little below 62 p.c.

Under these conditions, and for these reasons, after several trials, the following formula and process were adopted:

Clean, well dried strophanthus seed 256 parts, (4 lbs. avoirdupois—)
Broken glass 128 parts, (2 " " —)
Stronger ether s.g. .725 at 15.6°C.
Menstruum of 2 parts alcohol s.g. .8145 at 15.6°C.
and 1 part water;—or alcohol of 62 p.c.,
or s.g. .8914 at 15.6°C. or .8853 at 25°C.—of each a sufficient quantity.

Grind the seed and glass together until the seed is cut into a fine, oily, fluffy powder; spread this out thinly, and dry it at about 110°F. or 43°C. Then pack it tightly in a percolator and percolate it with the ether until this passes free from oil. The ether is then distilled off for use again with another portion, and the oil is found to weigh 60 parts (15 ounces). Then again spread the powder out, dry and weigh it. It will now, including the weight of the 60 parts of the oil, be reduced to about 242 or 243 parts (3 pounds 12½, to 3 pounds 12¾ ounces), and this is to be taken as the weight of seed upon which to adjust the yield of tincture,—5 parts to 84 by weight. Repack this powder in the percolator and percolate it slowly until 4082 parts (64 pounds) of tincture is received. (This 64 pounds of tincture, according to the temperature at which it is measured, will measure 69 to 71 pints.) This tincture will be practically identical with that yielded by the original British process of Mr. Wm. Martindale, of London.

The seeds as received contain a very variable amount of moisture, and, therefore, a tincture of uniform strength cannot be expected, unless they are well dried. A lot of 20 pounds of good seed lost in the preliminary drying 1 pound 8 ounces, or 7.5 p.c., and in the second drying after being powdered and exhausted with ether they lost about 5.1 p.c. more. The powdering with the glass appears to be best done in an iron mortar, and to do it well is a tedious undertaking. Without the glass, either in a mortar or in any ordinary mill, an oily paste or cake is the result. With the glass the whole is brought to an oily, fluffy powder, which cannot be got through a sieve. The powder should be dried well before the application of the ether, because if water be present the ether extracts a small proportion of the active principles. The packing for the ether percolation should be very tight, and the ether be passed through slowly. About 1150 parts (18 pounds) of ether is required to reach a point where a few drops of the percolate evaporated from a watch glass leaves no oily film. The ether is recovered by distillation, but is fit only for the same use again. The amount of oil from processes of 4 avoirdupois pounds of dried seed is pretty uniformily about 15 avoirdupois ounces or nearly 23.45 p.c. Although this apparently very liberal use of ether seems to extract all the oil, it really does not do so, for when the tincture is cooled down to 15.6°C., it becomes slightly cloudy from precipitation of oil. When stronger alcohol is used, this, of course, does not occur, but the oil is there in equal amount in both cases. The fact that when the powder is again dried, after the ether, it loses over 5 p.c.

in weight, is a sufficient reason for this third drying. And as that which is thus lost, is certainly not seed, the proportion of seed to tincture is adjusted by the weight after this loss, as a means of reaching uniform results in the strength of the tincture. The second packing for the alcohol percolation must not be very tight, but must be carefully done, and the percolation must be slow. Even with great care, and with all this menstruum, the exhaustion is not complete, and there is almost a necessity to pass, say, 15 or 16 pounds more of menstruum through the seed of a 4 pound portion, and use this weak percolate as so much menstruum at the commencement of the next percolation.

The percolating to a given weight of tincture rather than a given measure, beside being far more accurate, is more convenient and easy, and less liable to mistake.

The finished tincture though entirely clear, on standing a week, deposits a very small stratum of a sticky black sediment which adheres to the bottom of the bottle, and from which it is easily poured to the last, no part of the tincture needing filtration.

The tincture is of a bright yellowish wine color. The odor is suggestive of mustiness, and the taste is rather persistently bitter. It is miscible with water in all proportions without cloudiness. The s.g. is .8931 at 15.6°C. or .8869 at 25°C. compared with water at these temperatures.

The commencing dose of this tincture is 5 to 10 minims, and a total quantity of 50 to 60 minims within any 24 hours is probably the limit of safety. For general purposes it is better to increase the frequency than the size of the doses until 50 to 60 minims in the 24 hours is reached, in case smaller quantities are not sooner effective. Its action upon the heart, arteries and kidneys must always be closely watched, and the doses varied in accordance with the effects. It is a very potent agent, but not a very dangerous one under any ordinary circumstances, and in careful hands is potent for good. Five or ten minims every two or three hours should, in three or four doses, yield definite effects in steadying and supporting the heart's action,—relieving the arterial tension,—that is, softening of the pulse,—relaxing and softening the skin,—and promoting diuresis;—and when these effects are realized, or fail to be realized, the proper indication for dosing is obtained, and the quantity used may be kept steady or be diminished or increased. Such care is necessary to realize the good that the agent is capable of, and with it no danger has yet been encountered.

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Vol. III. No. 5.

AN EPHEMERIS OF MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

APRIL, 1890.

BY
EDWARD R. SQUIBB, M. D.
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CHARLES F. SQUIBB, A. B.

BROOKLYN, N. Y.
1890

NOTICE.

These pamphlets have always been issued without charge, and although they were sent out for a few years with fair regularity, they are now very irregular and infrequent, and may at any time cease altogether. No one need write to know why he does not receive them more regularly or more frequently, because if he has not changed his address, all will have been sent to him, and much time is required to answer such letters.

A list is kept with care of all who are supposed to be specially interested in Materia Medica and Pharmacy, and however irregularly and infrequently these pamphlets are published, one copy of each issue is mailed without charge to each name on the list, and the list is, as it has always been, freely open to new names that may desire to be upon it.

But after an issue has been distributed, neither copies of that nor any other back issue can be sent free of cost, and all orders, to receive any attention, must be accompanied by ten cents in postage stamps or postal note for each pamphlet wanted.

The two completed volumes, separately bound in cloth, are still accessible to any who may want them and will remit $1.16 for each or for either volume. On receipt of the money they will be mailed postage paid.

AN EPHEMERIS

OF

MATERIA MEDICA, PHARMACY, THERAPEUTICS AND

COLLATERAL INFORMATION.

VOL. III. APRIL, 1890. No. 5

THE APPROACHING REVISION OF THE UNITED STATES PHARMACOPŒIA.*

The United States Pharmacopœia, in common with other laws and standards, originated in the necessity for it. It was not created by law, has never had the support of law, nor has it ever asked for it, but was formed upon the experience and example of other countries within and by the medical profession of this country. It originated in the New York County Medical Society, in January, 1817, upon a design and proposition of Dr. Lyman Spalding to prepare for and call together a general convention of delegates from incorporated medical bodies to meet in Washington on January 1, 1820. This convention met at the time appointed and constructed and published the first Pharmacopœia of the United States of America, then commonly called "The American Pharmacopœia." There had been other local pharmacopœias before this, and probably the first of these was a small book of 32 pages entirely in Latin, for a military hospital of the U. S. Army in 1781, "adapted especially to our present state of need and poverty which we owe to the ferocious cruelty of the enemy, and to a cruel war brought unexpectedly upon our fatherland."

A much larger and better work was, however, done in "The Pharmacopœia of The Massachusetts Medical Society," published in 1808; and in 1816 the Pharmacopœia of the New York Hospital was published. But these all seemed merely to express the need for a national pharmacopœia, and on the appearance of the U. S. Pharmacopœia of 1820 they all seem to have been abandoned.

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*Read as the annual address before the Kings County Medical Association, February 14th, 1890, by the retiring president, E. R. Squibb, M. D.

Although the U. S. Pharmacopœia has never had any legal authority, it has always had a legal standing in being respected by the courts of law, and it has generally been admitted as standard authority in legal decisions within its scope.

Originating in 1820, it has been regularly revised six times, or once every ten years, since that time, and it has been the good fortune of this writer to have participated in four of the revisions, and to have served in three. The original construction of the decennial convention was by delegates not exceeding three in number from all incorporated State Medical Societies, incorporated Medical Colleges and incorporated Colleges of Physicians and Surgeons throughout the United States, and this construction held good up to the convention of 1850, when for the first time delegates from incorporated Colleges of Pharmacy were invited. This important step of progress amounted to a reformation in the work, and the introduction of this element into the conventions and their committees has so much extended and improved the work in material as well as in detail, that the advent of pharmacy must be regarded as the most important step taken in the sixty years of progress. And, so long as a just balance can be maintained between the elements of medicine and pharmacy, so that each may check the other within its proper prerogative, the Pharmacopœia is sure to be progressive and successful. With the medical element in excess it will tend to go back to the original condition of a materia medica catalogue, but with the pharmacy element in excess it will do much worse, for then it will tend to become a trade adjunct. That is, the pharmacy element being more mercantile in its character than medicine, and farther removed from the issues of life and health, is less safe for the true interests of a pharmacopœia. A pharmacopœia, in the true interests of the art of relieving suffering, had much better be a mere catalogue of simple substances than a complex mass of polypharmacy, but should be neither the one nor the other, and need be in no danger of either the one or the other, provided a just balance be maintained between the two natural subdivisions of the one inseparable interest.

In the convention of 1850 another step of progress was made by inviting the heads of the Medical Departments of the Army and Navy to participate in the conventions. In the conventions of 1860 and 1870 these departments appeared by one delegate from each; and in that of 1880 the U. S. Marine Hospital Service was added, thus giving more strength to the medical branch of the interest. If a just balance in ability as well as in number of delegates can be maintained in these conventions, there can be no great danger to the interest involved, even though a preponderance of the medical branch would be the safer. But there has been an unfortunate tendency in the medical profession to neglect or overlook that interest, while the interest of pharmacy is carefully stimulated and kept at its best. Medical delegates are appointed by comparatively few of the organizations appealed to, and the appointments which are made are often made without special selection, and even in a careless perfunctory way, whilst all the pharmaceutical organizations are fully represented by their best men, and their delegates very generally attend and are active in the proceedings. Under these circumstances it seems very desirable that the medical profession should awake to more care of this most important of all its general interests, if it would avoid the danger of losing the interest by having it perverted.

In discussing the proper mode of revising a pharmacopœia, it may not be amiss to glance at the plans pursued by other nations. It happens that just now two of the most important pharmacopœias of the world are being revised,—those of Germany and Great Britain.

The German Pharmacopœia is in process of revision, and nearly completed by a Commission which consists of twelve physicians, two Army surgeons, six chemists, six pharmacologists and seven pharmacists or thereabouts, all appointed by the Government, and they are understood to have done the work mainly by sub-committees who report to the general sessions of the Commission; and it is understood that very little of the work,—old or new,—is accepted on other authority than that of actual trial under control of the Commission. As an illustration of what the Commission has provisionally done, the " Pharmaceutische Zeitung," Vol. 34, No. 101, page 766, Berlin, December 18, 1889, gives the following notice :

Articles dismissed from the present Pharmacopœia are 77 in number, including 9 extracts, 11 tinctures and 4 ointments. In this list are two articles, Aloes and Camphor, the dismissal of which will not be understood here.

Of the articles proposed for admission to the new Pharmacopœia, 88 have been rejected. Among those rejected we find several that have some popularity here. For example, it will surprise many to find that the following articles have been weighed in the German balance and found wanting: Amylen Hydrate, Apiol, Boroglycerin, Creolin, Eucalyptol; Fluid Extracts of Cascara Sagrada, Castanea, Damiana, Gelsemium, Cotton Root, Grindelia, Hamamelis, Corn Silk, Wild Cherry, Sarsaparilla and Black Haw; also, Hypnon, Lanolin, Methacetin, Nitroglycerin, Pyridin, Saccharin, Somnol and Sulphate of Spartein.

The British Pharmacopœia is controlled by a committee of "The General Council of Medical Education and Registration of The United Kingdom." At the last revision of 1885 the Pharmacopœia Committee consisted of eight members, all in the interest of the medical profession, and the Committee employed Professors Redwood, Bentley and Attfield as Editors of the Pharmacopœia. In December last this committee reported to the Council that 20,000 copies of the Pharmacopœia of 1885 had been printed, of which only 559 remained, and recommended the printing of 3,000 additional copies. The committee also recommended that an addendum to the Pharmacopœia of 1885 be prepared by Dr. Attfield, under the direction of the Chairman of the Committee and another member, with the understanding that no new remedies are to be introduced into it except such as have met with general approval. This recommendation was agreed to by the Council, and it is understood that the work is now in progress. This is the way in which the B. P. of 1867 was revised in 1874. There was a new B. P. in 1885, now to have an addendum in 1890.

Through this ultra conservative policy the British medical profession by authority of the government has jealously guarded that Pharmacopœia from any direct influence of British pharmacy, while indirectly availing itself of the highest pharmaceutical ability by employing some of the best men to do the detail work and calling them editors. That the pharmaceutical interest of Great Britain is justly entitled to a recognized or official share in their Pharmacopœia for the best interests of the Pharmacopœia itself, can hardly be doubted, and yet it cannot be denied that the Pharmacopœia as it stands is of excellent quality; and is, as a standard, more closely followed and more generally used in British medical practice than any national pharmacopœia.

The Convention for the Revision of the U. S. Pharmacopœia of 1880 adopted the following resolutions for calling the Convention of 1890:

Resolved, That the President of this Convention shall, on or about the first day of May, 1889, issue a notice requesting the several incorporated Medical Societies, the incorporated Medical

Colleges, the incorporated Colleges of Pharmacy and incorporated Pharmaceutical Societies throughout the United States, and the American Medical Association and the American Pharmaceutical Association, to elect a number of delegates, not exceeding three, and the Surgeon-General of the Army, the Surgeon-General of the Navy, and the Surgeon-General of the Marine Hospital Service, to appoint, each, not exceeding three medical officers, to attend a General Convention for the Revision of the Pharmacopœia of the United States, to be held in Washington, D. C., on the first Wednesday of May, 1890.

Resolved, That the several bodies, as well as the Medical Departments of the Army, Navy and Marine Hospital Service, thus addressed, shall also be requested by the President to submit the Pharmacopœia to a careful revision and to transmit the result of their labors, through their delegates, to the Committee of Revision, at least three months before the meeting of the convention.

Resolved, That the several medical and pharmaceutical bodies shall be further requested to transmit to the President of this Convention the names and residences of their respective delegates, as soon as they shall have been appointed; a list of whom shall be published, under his authority, for the information of the medical public, in the newspapers and medical journals, in the month of March, 1890.

Resolved, That in the event of the death, resignation, or inability of the President of the Convention to act, these duties shall devolve, successively, in the following order of precedence: upon the Vice-Presidents, the Secretary, the Assistant Secretary, and the Chairman of the Committee of Revision and Publication of the Pharmacopœia.

This call was published by the President of 1880 in almost, if not quite all the medical and pharmaceutical journals of the United States, and seems to have awakened much more attention in the pharmaceutical than in the medical bodies to whom it is addressed.

It should be noticed that here, for the first time, the American Medical Association and the American Pharmaceutical Association are requested to elect delegates; and also for the first time the three medical departments of the general government are officially requested to appoint delegates. Again it should be noticed that the several bodies addressed, including the Army, Navy and Marine Hospital Service, are requested to submit the Pharmacopœia to a careful revision and to transmit the result of their labors to the

Convention of 1890, through their delegates, and as thus provided for, the Convention will meet in Washington on May 7th.

These Conventions have in the past decided upon the general principles which were to control the revision, and then have appointed Committees of Revision to carry out these principles, and do the resulting work in detail; and in view of the very great importance of these Conventions and their Committees of final revision, a more general knowledge of what is to be done by them may be useful.

Each Convention has been organized under the officers and by the rules of the one preceding it,—a Committee on Credentials appointed, and when the authorized delegates have been admitted, a Nominating Committee is selected by the several delegations, one member from each delegation, including those of the Army, Navy and Marine Hospital Service. This Committee nominates permanent officers of the Convention for the decennial period, and when they are elected, the minutes of the last Convention are presented. Next, the report of the Secretary of the Committee of Revision and Publication of the last Pharmacopœia is presented. Next, the preliminary revisions sent in by the different bodies, and any other written communications and contributions are called for to be referred to the new Committee of Revision and Publication.

The Nominating Committee is then instructed to nominate a new Committee of Revision and Publication, the size of such Committee being decided by the Convention. The last Committee was 25 in number.

The last Nominating Committee was also instructed to report a plan for revising and publishing the Pharmacopœia; and to make provision for the revision of the Pharmacopœia in the future.

Then the powers and duties of the Committee of Revision were defined, and the Committee duly authorized; and this done, the general principles to be followed by the Committee in the new revision were discussed, and either adopted or rejected. This is really the most important part of the work of the Convention, as will be seen by a brief review of the headings as they appear in the Proceedings of the Convention of 1880. First, after due discussion, it was decided that all officinal titles should be given in both Latin and English, but that the text be in English. Then it was decided that the entire Pharmacopœia present an alphabetical order of titles, classes, and titles under classes; that synonyms in common use be given; and that at the end of each article the names of all the preparations into which it entered should be given. Upon these points the experience of ten years has been so favorable that it is hardly likely they will be disturbed or be subjected to much adverse criticism.

The directions for the description of crude drugs seem also to have been sufficient and satisfactory in the main, but in a few instances they do not seem to have been fully carried out by the Committee. This point may lead to discussion in the Committee, but probably not in the Convention.

The directions for the description of chemicals have of late excited much important discussion. It is directed that Opium and Cinchona shall have detailed processes of assay for the alkaloids, and that the minimum percentage of total alkaloids required be given under Cinchona, and the minimum and maximum of morphine in Opium be prescribed. No fault has been found with these directions, but it has often been claimed with much force, that now processes of assay should be directed for all the important crude drugs, even including those which have no definite, separable, active principles. This claim seems to be an outgrowth of experience obtained by the leading step taken in regard to Cinchona and Opium, but this is certainly not the case, for no one who has had much experience with Cinchona and Opium assays can have escaped the difficulties and uncertainties of these. The assaying of crude drugs for their active principles seems an easy matter to those who only read and write upon the subject. But those who attempt to practice the processes soon get a very different impression, for there is really nothing more precarious and uncertain than these assays in general hands with but a small experience in such work. Assay processes might perhaps be wisely directed for a few additional drugs such as Aconite, Belladonna, Conium, Hyoscyamus, Ipecacuanha, Jalap, Nux Vomica, Scammony and Veratrum Viride.

Pharmacopœial processes of assay will be successful or unsuccessful in proportion to their character. If they aim at a high degree of accuracy and precision they must, necessarily, be elaborate and complex to a degree that places them beyond the reach of general pharmaceutical ability. But if they aim at only the very moderate degree of accuracy, such as satisfies the careful manufacturer in the selection of materials, rough processes of approximate assay may be found that are sufficiently easy of application to be successfully applied to pharmaceutical ability and usage through the authority of the Pharmacopœia. While most of these rough and ready processes are secreted in the hands of manufacturers, yet enough of them are published to give the Pharmacopœia opportunities of selection in these, and in the trials for selection similar processes for all would be naturally reached. Including Cinchona and Opium eleven drugs have been named which might have processes of assay given in the Pharmacopœia, and if high degrees of accuracy be not aimed at, a moderate amount of work in the selection of proper menstrua would enable the Pharmacopœia to apply the shaking out process to all these articles with results sufficiently close for the present scope of the Pharmacopœia,.and sufficient to prevent the Pharmacopœia from depending upon either experts, manufacturers, or commentaries. For example, a simple and easy process for Opium assay, which in hands of ordinarily educated pharmaceutical skill and ability would have a maximum range of probable error of not more than a half of one per cent. above or below the truth,—might be better adapted to the pharmacopœial usage of the present time, than a critically accurate chemical process with a range of error of a tenth of a per cent. ;—first, because no two samples of the same lot of Opium, whether moist or in powder, would come within this small range of error; and next, because such a process would require a degree of expert knowledge and skill rarely found in pharmaceutical practice.

Another important consideration not to be overlooked is, that with the exceptions of Cinchona, Jalap, Opium and Scammony, the drugs named can always be bought by pharmacopœial description and tests, of such quality as to yield preparations of practically uniform therapeutic value. The claim frequently heard that all pharmaceutical preparations from crude drugs should be made or adjusted by assay is so plausible and attractive, as to form a most fertile basis for specious advertising by manufacturers of these preparations, and if the Pharmacopœia could be committed to this or any similar doctrine it would put much money into the pockets of large manufacturers, and just to that extent would divert practical pharmacy from its legitimate channels and proper responsibilities. In the first place, the claim is untrue and unfair because a very large proportion of important drugs have no separable active principle that can be determined by assay, and therefore their quality cannot be determined by assay, nor can their preparations be adjusted by assay. Out of some ninety officinal drugs in all, there are about thirty-four of the more important ones which may be fairly represented by Ergot, Rhubarb, Senna, Wild Cherry, Dandelion, Columbo, Gentian, Butternut, Pareira, Cotton Root, Cimicifuga, Buckthorn, Leptandra, Sarsaparilla, Spigelia and Stillingia, which could not be adjusted by any ordinary processes of assay, and which do not need it if they could, because care in buying them by pharmacopœial description and tests, rather than by price, will always easily obtain a uniform good quality, at moderate cost. Again, while a fair degree of accuracy and uniformity in the strength of galenical medicines is most desirable, any strain after a degree of accuracy that is not necessary, nor available if attained, is hurtful by whatever is sacrificed to attain it. In the therapeutic uses of medicines, doses are anything but definite or accurate in quantity. Of the same medicines different individuals require different doses to yield the same effect. And even the same individual requires different quantities at different times and under differing conditions, and the real dose is always that variable quantity that yields the peculiar effect of the agent. How then can the physician avail himself of any degree of critical accuracy beyond that practical uniformity of strength and quality upon which his experience is based, or of any degree of critical accuracy which is beyond the limit of accuracy determined for him by variable individual susceptibility ? All that is true and sound on this point is that a practical degree of uniformity is all that can be useful, and that this can be attained by the Pharmacopœia without any such system of elaborate assaying as would tend to throw this important interest of the Pharmacopœia into the hands of experts, or would-be experts. The line of wise action seems not difficult to draw here. If the descriptions and tests of the Pharmacopœia can be improved without carrying them beyond the reach of educated pharmaceutical or medical skill in application, this should be done, applying assay processes only to such drugs as have easily separable active principles. Then, a very few preparations, such as those of Opium, Nux Vomica, and perhaps Cinchona, might wisely have their strength adjusted by these assays. There has never been a time within the forty years' experience of the writer, when officinal drugs were more accessible to those who would take the trouble to look for them, and be willing to pay for them; and to those who will not take the proper pains, nor pay adequate prices, the Pharmacopœia would continue to appeal in vain, even by the most elaborate system of assays and adjustments, if such a system was practicable.

The Convention of 1880 next specified the chemical formulæ and chemical notation that were to be used throughout, and also directed special chemical processes to be given in detail for officinal chemicals, with the result that these have been, in the main, fairly successful. Some of the processes have not been given in sufficient detail, but such being now known, they will doubtless be amended.

A very important direction, given by the Convention of 1880, after much careful discussion and deliberation, was that, "All measures of capacity shall be abandoned and quantities shall be expressed in *parts by weight;* except that in the case of Fluid Extracts, the Committee of Revision and Publication shall have authority to adopt such process or processes as shall seem to it best."

This change has caused some popular dissatisfaction and adverse criticism, and it is not unlikely that in the approaching Convention there will be an effort made to get back to the old weights and measures on the one hand, or to metric weights and measures on the other. The present plan having now been in use for about eight years, there should have accumulated experience enough to enable it to be dispassionately discussed, and if it be so discussed, it will doubtless be continued in force. The chief objection to the plan seems to be the weighing of liquids which had hitherto been measured. The writer has looked in vain for any arguments against the weighing of liquids. The reason why the practice was changed was that the measuring of liquids was inaccurate beyond what is easily controllable, and beyond what is now admissible in the progress of medicine and pharmacy. No reasonable person doubts this, and no attempt to fairly controvert it has been noticed in any other way than by the mere clamor that weighing liquids is too troublesome, and, therefore, the less troublesome measuring must be reinstated. No one has ventured to say that the measures accessible in general practice are as fairly accurate or uniform as the weights are ; nor, that if the measures were accurate, measuring by them would be as accurate, or anywhere near as accurate as weighing. Every one knows that the adjusting of the level of the liquids to the mark in measuring is never twice the same even in the same hands, and that with double the amount of care and pains in measuring, the weighing is the more accurate. Every one knows, too, that, as measuring must of necessity be continued in use for dispensing and dosing, and is there applied only to dilute liquids when small errors may be tolerated,—this circumstance limits the weighing of liquids to the actual practice of the Pharmacopœia; and the number of times when, in compounding from the text of the Pharmacopœia, liquids require to be weighed, is small though very important. Those who object to the weighing of liquids simply because it is troublesome and inconvenient, while granting the superior precision of the practice, cannot certainly be of the same class which demands to have preparations adjusted by assay for the sake of precision.

Objections have also been raised against the use of parts by weight, and it is not unlikely that efforts will be made in the Convention to return to arbitrary weights. This, again, would be to lose all the ground gained by eight years' experience in this step of modern progress. The chief reasons for adopting this simple and precise method of expressing relative quantities were, first, that it avoided the two tables of weights and measures which had led to confusion for so many years, and allowed the operator to use any system which he might have at hand, including the metric system; and second, that it did not commit the Pharmacopœia to any definite quantity for its preparations, but allowed the operator to make the quantities that were best adapted to his wants at the time. That is, he might construe the parts by weight to be any system of pounds or ounces he might have, or he could make each part a half or a quarter ounce, or ten grains or one grain, or a gram., or kilogram, and the result would be always the same. Besides it was a step towards the metric system, the adoption of which though distant must now be considered very sure. To return to the old apothecaries' weights and measures, or to adopt the avoirdupois, would be to lose all that has been gained, and throw the labor on some future convention of starting anew from the same old point of ten years ago. The reasons for making this change to parts by weight have never been successfully controverted. No one has ever shown that the change did not accomplish the objects intended by it, nor has any one shown that the change involved disadvantages which, either in their nature or degree, overbalanced the advantages. The summing up of all that has been said against the method seems to have been that it was not generally understood sufficiently well to be generally adopted, while it replaced a method that was well understood and successfully practiced, and therefore it was inconvenient and objectionable. Thus stated, these objections seem simply puerile, especially if looked at in connection with the examination papers of the various schools of the country year after year. That any of the students who passed any of these examinations for the last ten years should not know enough of common elementary arithmetic, to easily substitute parts by weight for any arbitrary system of weights and measures with the tables before them, is incomprehensible. Then it must not be forgotten that the former revision adopted the apothecaries' or 480 grain ounce, and the 456 grain fluidounce, while it was shown that ignorance, stimulated by pecuniary profit, led to the not uncommon use of the 437½ grain ounce and fluidounce, and to this day some of the largest manufacturers in the country graduate their measures by the 437½ grains of distilled water to the fluidounce. Should there be any thought in the Convention of going back to an arbitrary system of weights and measures the avoirdupois table should be adopted, as in the British Pharmacopœia, where the small ounce and fluidounce are used exclusively. Then, in such a change as this it should not be overlooked that most troublesome calculations and equally troublesome fractions would be required to keep the officinal preparations near their present strength.

In concluding these remarks, it may not be useless to offer the force of one single example. It is highly probable that this writer uses the Pharmacopœia in actual practice as much as any other individual in this country, and he has found the weighing of liquids, and the use of parts by weight, not only more accurate, but also much more convenient than the older usage, and he is, therefore, a strong advocate of the continuance of the plan in the approaching revision.

The last convention gave wise directions, that such preparations as tinctures, wines, etc., in which slight variations are not important in case of a change for uniformity's sake, might be reduced to uniform percentage strength, but, that the more active preparations of this class should remain, as nearly as possible, unchanged. The work of the Committee of Revision under these directions has been satisfactory so far as is known.

The direction that temperatures should be expressed in both centigrade and Fahrenheit degrees was very wise, and the practice has been very useful.

The direction that all doses shall be omitted from the Pharmacopœia was but a continuation of the usage in all previous revisions. In every revision there have some efforts been made to have maximum and minimum doses given, as in some other pharmacopœias. This has been advocated, not only as a guide to physicians in the use of both old and new medicines, but also as an important guide to pharmacists in checking mistakes in prescriptions, and in exercising caution against excessive doses. It has also been advocated as tending to increase the usefulness and authority of the Pharmacopœia in courts of law. But the objections, which have always prevailed as overbalancing these admitted advantages, were first that, in any accurate sense, there are no maximum and minimum doses that are not so wide apart as to lose all practical value, and be in danger of misleading. It is generally known that each individual has a different susceptibility to potent agents, and therefore requires a different dose. Next, that different diseases and disorders require different doses; and different conditions of the same disease also require different doses. And, finally, that different authorities differ so much among themselves, that from them it would be impossible to adopt a standard range of doses that would be short enough to be of much practical value, while the Pharmacopœia, aiming to be a standard, could not be a standard in this. In short, the only doses that could be wisely stated would be those proper to begin with, imposing on physicians their duty of watching the effects of their agents and increasing their doses until they reach the desired effects or the physiological effects. Undoubtedly physicians are often so trammelled by stated doses as to miss the uses and effects of their agents, and if this be so, and if the above considerations be admitted, then all that the Pharmacopœia could wisely do would be to give proper, safe doses to begin with in the application of its standard agents. This much would not commit the Pharmacopœia to anything beyond its legitimate scope.

The Convention of 1880 directed a large number of useful tables to be appended to the Pharmacopœia specifying those most desirable, and authorizing the Committee of Revision to add any other tables that might be deemed expedient. The Committee did add a number of very important tables selected with care from various authorities. But three of those directed by the Convention were omitted. One of them, namely, a weight and volume table to facilitate the use of parts by weight, and by the metric system, is very important, and would have been very useful. The want of such a table has been supplied by the commentaries on the Pharmacopœia, but just to the extent that this is necessary or useful do the commentaries take the place of the Pharmacopœia. Such a table involves a large amount of careful labor in both construction and detail work, but it seems to be practicable, inasmuch as the commentaries have supplied most of the elements of such a table in detail.

Another table ordered by the Convention and not supplied by the Committee was one of the specific gravities of officinal liquids for each degree of temperature between 10° and 25°C. (50° and 77°F.) This would be a very useful table indeed, and one that, so far as this writer knows, is not to be found elsewhere, but it is one that would require much careful labor to make. Specific gravity is perhaps the most important of all the tests of quality of liquids, as it is the most generally applicable, and the main difficulty in the way of its application has always been the adjustment of the liquids to a single given temperature. Therefore, if a table was carefully constructed giving the equivalent figures for each degree, or each five degrees of ordinary room temperature, specific gravities could be so easily, so quickly and so accurately taken as to very greatly increase the application of this test. Such a table might be constructed in either of three ways. The standard volume of water for comparison might remain constant at 4°C.=39.2°F., or might remain constant at 15.6°C.=60°F., or it might vary with the room temperature at the time of weighing. That is, the volume of water for comparison might always be at the same temperature as the liquid compared. This latter is the true, essential idea or principle of specific gravity, but its general use would involve the necessity of either a special bottle with a graduated tubular stopper graduated for each degree or five degrees of water expansion,—or a troublesome arithmetical calculation,—both very objectionable when the aim is easy, rapid and accurate practice. Apparent specific gravity by either one or both of the fixed standards would be preferable. Throughout continental Europe the standard volume most used is water at 4°C., and this is becoming common in Great Britain and in this country also, but for a true specific gravity by this standard, the liquid compared must be reduced in temperature to the standard 4°C. This is always troublesome, often difficult, and sometimes impracticable, and therefore apparent specific gravities by this standard are common. That is, the standard volume at 4°C is used, and the temperature at which the same volume of the compared liquid is weighed, is given. As a general rule, throughout Great Britain and this country the standard volume used is water at 60°F.=15.6°C., but the last Committee of Revision very unwisely, as the writer thinks, adopted a new standard temperature of 59°F.=15°C., so that now the officinal specific gravities cannot be referred for comparison to any known tables in previous use with perhaps a single exception. If a table had been constructed as directed by the Convention this would have been the less objectionable, because then the new figures could have been easily compared with those of previous usage, and the equivalents be known. The most convenient usage for a pharmacopœial table at the present time would doubtless be to adopt 15.6°C.=60°F. as the standard volume and take this as the basis of a table of apparent specific gravities. That is, let the standard temperatures remain constant, and compare all the other temperatures with this. This method would be almost necessary in this country, as almost all the specific gravity bottles in pharmaceutical use here are adjusted with more or less accuracy to 60°F. Then all that would be needed would be to fill and weigh the bottles at any room temperature, at which the liquid might be. Then ascertain this temperature and by it refer to the table where, coupled with the apparent specific gravity at this temperature, would be found the true specific gravity at the standard temperature. In constructing such a table the actual specific gravities should not be taken closer together than for each 5°C., because the interval could be more accurately filled in by calculation than by observation. If such a table be not supplied in the next revision there should at least be given, in all cases, an apparent or true specific gravity at 25°C.=77°F. as is now done in the instances of Ether and Alcohol.

The third table ordered by the Convention but not supplied by the Committee, was one comparing the strength of powerful galenical preparations of foreign pharmacopœias used in this country with that of the corresponding preparations of our own. Such a table would be useful, and occasionally important. But such comparisons are of late so infrequently needed and so easily reached, when needed, by a little calculation, that the table has probably not been missed.

Knowing, as this writer does, the enormous labor put upon the last Committee of Revision by the Convention, and the great and numerous difficulties under which this work had to be done, it is not to be wondered at that some of the less important matters were left out. The next Committee will, it is hoped be under much more favorable conditions. Thanks to the wisdom by which a high price was put upon the Pharmacopœia, there is now money enough in hand to begin the new revision and carry it forward for some time without delay. The last Committee had no money, and although the Convention authorized the employment of experts for the detail work, it did not provide any money to pay such experts, so that it was only when the work was so nearly done that the copyright could be sold, that money became available, and then experts were not needed. All the work had to be allotted to the members of the Committee, and it was done by them, busy men as they were and are, without any remuneration of any kind. The Chairman of the Committee, however, had far the most laborious position, and a position that no future Convention should ever ask a chairman to fill without liberal compensation, for his ability, time and work. These Conventions must have Chairmen of exceptional ability and indefatigable industry, who can give a large portion of their time to the work, and such a Chairman who has served once has, to the Convention, double the value of any new man whose peculiar and rare qualifications for the work are unknown and untried.

There has been a good deal said in the journals against the high price of the present Pharmacopœia, and in favor of a book of low cost, and it seems to have escaped the attention of the writers that this was the only way in which money could have been raised then to defray the absolute outlay necessary for a proper revision of a national pharmacopœia, even when all the individual labor of the revision was volunteered without remuneration by men who could ill afford it. And the profit upon the sale of the Pharmacopœia must be, in the future, the only means of paying for the labor put upon it. Besides, it must be borne well in mind that the amount and quality of the labor put upon it will be sure to govern the demand for it, and that the time has gone by when the kind and quality of labor that will make a salable book can be had without being paid for. There are several private interests which would be willing to take the work and pay all expenses upon it, and then give the book away, if they might have its authority and prestige to use for business advertising purposes, especially if it could be made to lean just a little in the direction of any one of the single special interests. But the number of those who would like to see the Pharmacopœia paid for, either wholly or in part, in any such way, must be very few. The price realized for the Pharmacopœia over and above its actual money cost, is in reality the tax which is paid by those who use it to pay the expenses of the next succeeding revision, and those who demand that it should be sold at or near cost, simply ask that the Convention and its Committee pay their own expenses beside contributing the time and work. Of course a line must be drawn somewhere, and the experience of the last revision will be very useful in determining the price of the next, but it must always be borne in mind that each revision is more expensive than the last, and that in no revision yet has the expensive part of the work been paid for. And, farther, that in all succeeding revisions it must be paid for if better work is to be had. The only way in which a really good Pharmacopœia, fully up to its time in the quality and quantity of the work put upon it, can be supplied at a low price, is for the Convention to pay the expenses by a tax upon the bodies whose delegates form the Convention. In other nations the governments pay all the expenses, including the expert skill and labor, yet in some of them,—Great Britain and France, for example,—the book is sold at a high cost for those nations. It is quite probable that now that a small surplus will be handed over toward the beginning of the next revision, and now that the copyright is worth more than ever before,—the approaching revision may be kept as good a book and yet be sold at a lower price, especially if the Committee should resolve not to sell the copyright, but instead, to publish the book themselves in case they cannot get a better price for it than heretofore.

By far the most important work of the Convention is the selection of its Committee of Revision and Publication. The Convention first decides of how many this Committee shall consist, and then how it shall be nominated. The last Convention directed that it should consist of twenty-five members, and be nominated by the Nominating Committee; that is, the Committee raised to nominate permanent officers for the Convention. This Nominating Committee consisted of thirty-eight members, or one from each body represented by delegates present, and one, each, from the Army, Navy and Marine Hospital Service, the several delegations being called upon to name their members. In regard to these two very important Committees in the approaching Convention the following points are offered for consideration in advance, and for whatever they may be worth :

The Convention of 1880 consisted of about 116 accredited delegates, or if duplicates and alternates be omitted, about 104,—69 medical and 35 pharmaceutical. About 80 of these were present, and therefore the Nominating Committee of 38 was nearly half the Convention. Such a Committee, though very fairly representative, is too large for the best committee work, and the next Committee, if made up in the same way, will probably be still larger.

In the selection of permanent officers for the Convention this Committee might wisely discuss the advantages of having the offices of President of the Convention and Chairman of the Committee of the Revision and Publication devolve upon one man, and of attaching a liberal salary to this office of ten years' duration of labor.

The Committee of Revision and Publication must of course select its own plan of work, but it would be entirely competent for the Convention, if it so pleased, to direct that every process and every test, including specific gravities, should be actually tried by expert hands before being accepted for publication. That is, that authorities on these points should not be accepted untried.

Again, it would be competent for the Convention, if it chose to do so, now that there will be a moderate amount of money to start on, with every prospect of a sufficiency in the future, to direct that under the guidance and control of the Chairman the detail work should be done by well selected and well paid experts, and be submitted to sub-committees for comment and confirmation, thus reversing the order of work in the last revision, where want of funds rendered such a plan as this impracticable. By some such plan as this every process and every test would have a double security for its accuracy, and would be, in this, a great improvement upon former revisions. Besides, it would very much lighten and simplify the individual labors of the committeemen, and give them more time for the consideration of admissions, rejections and other changes, which require much reading up and careful deliberation.

The recent introduction to the materia medica of synthetic chemical substances, which are either patented or trade-marked, seems to indicate that, although the substances are already numerous, they are still to become more numerous and more complex and confusing to the ordinary physician, and that no work of the Pharmacopœia is more important than to protect such physicians against the interested representations of trade in these very lucrative articles, if any of them should be admitted. The question as to their admission, and as to how many of them, is a most important one for the Committee, and one not to be lightly nor hastily settled. One difficulty in regard to these substances is comparatively new. Their chemical names are long and impracticable. Rational names are not easily, while empirical names are very easily found, and these are trade-marked or patented, and the tendency now is to trade-mark these rather than to patent them, because patents expire in a definite time, but trade-marks continue to protect indefinitely.

In conclusion, the writer begs to lay all possible emphasis on the grave importance of this work to the medical profession and to urge the need of sending the best and most conservative men to take active part in this Convention, remembering that inactive delegates, though in a numerical majority, carry little weight in Conventions of active men full of the spirit of mercantile enterprise.

BOSTON OPIUM AGAIN.

Another new and promising mercantile enterprise has been added to the many such that now invite the attention of shrewd dealers in the drug business. The supply of Boston Opium no longer depends upon the foreign manipulators. In their delicate and close processes for making it, these manipulators would occasionally get it a little below the lawful 9 per cent. of morphine, and then it was excluded from this country by the Custom House. Then a few shipments sent back to them took off or reduced the profits on those which got through, so as materially to damage the enterprise. But now a remedy for this has been found. One of the foreign makers of Boston Opium has come to this country and has associated himself with a capitalist in New York city who has been long in the opium trade, with a formerly large importing house. They import good natural opium, and the poppy leaves and other materials needed in their business that cannot be had here, taking care of the original foreign cases, so far as these will go, and thus equipped they manufacture what they are pleased to call Standardized Opium, to order and for the market, of any strength that may be ordered, keeping up the same handsome appearance as in the original Boston Opium. Of course this does away with the 9 per cent. Custom House limit and all the risks attending it, and supplies the market, under the very attractive title of Standardized Opium, with opium of any degree of dilution that may be ordered, and of appearance far better than natural opium. Already the writer has heard of cases of this opium that were ordered to contain 8 per cent. of morphine, which were found on assay to contain only about 6 per cent., and there is now really no limit, and no way of valuing this handsome opium short of an actual assay.

In sending this news to the large and influential Constantinople house of Messrs. Ihmsen & Co., the writer suggested as a partial check upon such practices, which were hurting their legitimate market very much,—that inasmuch as the appearance of this opium in contrast with the natural drug, was the principal agency next to price, in selling it, a remedy might be found in getting the producers of natural opium to improve the appearance of their product so as to compete, in this respect, with the adulterated opium. But these gentlemen think that it is only a question of a little time and experience among the actual consumers for them to find out how much better the natural opium is for their purposes in the long run. This very rational and conservative policy will hardly remedy the evil in this country,—at least not in any reasonable length of time with the expert skill, and money interest of the dealers against it.

There really seems to be but one effective way of meeting this difficulty with a prospect of checking the practice, and that is to—

BUY AND SELL OPIUM BY THE UNIT OF MORPHINE.

There are already a large number of articles in the market that are thus bought and sold, and Cinchona barks are prominent examples, and a good illustration of the practice, only that here the unit of value is crystallized sulphate of quinine instead of quinine. This complex unit instead of the simple and real unit of alkaloid, became so well established before its disadvantages were realized, that now it would be difficult to correct it. But in the instance of opium the unit should be either the crystallized or anhydrous alkaloid morphine.

Nine per cent. opium at $3.50 per pound by the case is equal to (3.50÷9=)39c. per unit of one per cent. Ten per cent. opium at $3.50 per pound would be (3.50÷10=) 35c. per unit. Eleven per cent. opium at $3.50 per pound, would be (3.50÷11=) 31.81c. per unit. Twelve per cent. opium at the same price would be (3.50÷12=) 29.17c. per unit. Thirteen per cent. opium at this price would be (3.50÷13=) 26.92c. per unit, and fourteen per cent. opium would be (3.50÷14=) 25c. per unit. This is about the range of natural opium in this market, and it gives a difference of

9 to 14 p.c., or 5 p.c. in morphine strength, and 39 to 25c. per unit, or 14 cents difference per unit in value. Taking the average of this range of 5 p.c. in morphine strength, as the standard unit of value, this would be 32c. per unit, and 9 p.c. opium would be worth (32×9=) $2.88 per pound;—10 p.c. would be $3.20 per pound;—11 p.c. $3.52; –12 p.c. $3.84;—13 p.c. $4.16; and 14 p.c. $4.48 per pound, a difference between the extremes of $1.60 per pound. The difference between these extremes in the Constantinople and Smyrna markets is never as great as this, though it occasionally approaches it, six shillings sterling per pound being about the limit of range there.

Now if the U. S. Pharmacopœia should adopt a fairly accurate process of assay for opium it would certainly soon become the standard for this country, and being fairly accurate the standards of other countries would not differ much from it. These opiums would simply be sold and bought at so much per unit, U. S. P. test, and the market fluctuations would be upon the value of the unit. An opium of 9 p.c. at 32c. per unit U. S. P. test would be $2.88 per pound. If of 10 p.c., $3.20 per pound. If of 11 p.c. (32×11=) $3.52 and so on. In this way only can opium be dealt in at its actual value, and each case, or each lot of five or ten cases would be accompanied by a certificate of assay. This assay would be so very small an addition to the price as to be quite unimportant in consideration of the value involved. For example, a case of opium of 150 pounds at $3.50 would be $525.00, and the assay costing $5.00 would be less than one p.c.

That powdered opium should be bought and sold by assay only is still more important, because almost all the powdered opium is used in medicine, and here the U. S. P. should be much more definite in morphine strength than it is if the therapeutic uses of the drug are to be considered. It now directs that powdered opium should contain not less than 12 nor more than 16 per cent. of morphine when assayed by the process given under opium. But it has been shown that this assay process has an inconstant error, varying between .75 and 1.25 p.c. below the truth, and practically this error has come to be considered as about one per cent., so that a powder testing 12 p.c. is accepted as containing 13 p.c., and this makes the officinal range 13 to 17 p.c. of morphine. This very large range of 4 p.c. is 26.6 p.c. of an average strength of 15, and the U. S. P. permits that a dose of its powdered opium, and of any of the preparations made from it, may be at one time nearly 27 p.c.

greater than at another—a variation that no intelligent physician would ever think of permitting in the standard for one of his most important agents if he realized what he was doing.

In drying opium for powdering it loses on the average about 20 p.c. of moisture, and thus each pound of moist opium is reduced in weight to about eight-tenths of a pound without the loss or injury of any of the morphine if the drying be properly done at a low temperature. By this loss a 10 p.c. moist opium becomes a 12.5 p.c. dry opium and yields a 12.5 p.c. powdered opium, and eight-tenths of a pound of powder has the actual morphine value of the original pound of moist opium plus the cost of drying and powdering, which is a process requiring about 6 weeks if properly done. Therefore, if the moist opium of 10 p.c. cost, say, $3.75 per pound for the .375 pound of morphine present in it, and the eight-tenths of a pound of powder containing the same quantity of morphine, it would have the same morphine value of $3.75 for eighth-tenths of a pound or what is the same thing (as 8 : 3.75 :: 10 :) $4.69. That is, its value per pound would have been increased by 94 cents. Then to this must be added the cost of drying, powdering, assaying and putting up in proper containers, and the interest, risk and profit on the money locked up during this six weeks' process. These charges aggregate not less than 21 to 23 c. per pound on the powdered opium and bring the cost up to (94+22=) $1.16 per pound on the original price of the moist drug, making the value of an opium costing $3.75 in the moist condition worth $4.91 per pound when dried and powdered. This $1.16 is a pretty constant figure and applies about equally to all grades and prices of opium when powdered from the ordinary moist condition of the markets.

Now the unit value of a 10 p.c. opium at $3.75 per pound is 37.5c. per unit, and upon this same opium when dried and powdered the unit value is (4.91÷12.5=) 39.3c. That is, it is increased in value by 1.8c. per unit, which is equal to 22.5c. per pound on opium of this assumed quality.

It therefore seems very simple and easy to quote moist opium at say 37.5c. per unit of morphine, or, 39.5c. per unit for the same opium powdered, making a difference of 2c. per unit between moist and powdered of the same quality. If the opium market rises or falls, then for every rise or fall of about 22.5c. per pound, the price per unit would rise or fall 2c. per unit.

It is only by the adoption of some such practice into the market, of buying and selling by a practically near approximation to the actual value that the gross adulterations of opium can be checked, or controlled for those who wish to avoid the adulterations. The adulterated or reduced opiums do not sell at correspondingly low prices, for then there would be no money in them, but being made attractive by external appearance they sell for much more than they are worth, and there is now no indication of poor opium so sure in this market as a handsome attractive appearance, and nothing would lead a morphine maker sooner to reject opium than this very handsome appearance, unless it was offered by actual test, and at a price correspondingly below that of natural opium. Nevertheless this adulterated opium actually brings within 25 to 35c. per pound of a natural opium that is worth from 80 to 90c. per pound more, and this 55c. per pound difference in price over actual value is the profit made by the adulterator.

This condition of market has now become so well established, and is so well known within the wholesale trade that no one there is deceived by it who is not willing to be deceived, or who does not make money by the deception, and if the medical and pharmaceutical journals would but take the matter up vigorously and earnestly, the retailers and consumers would soon be so well informed that they could not be deceived without knowing the deception. Unfortunately, however, the journals have, from some unknown reason, touched the subject but rarely, and very lightly.

The National Wholesale Drug Association have condemned the adulteration specifically, and by resolution decided to obstruct and oppose it. But this was as a National Association. The individuals composing the Association are the principal dealers in the adulterated drug, defending themselves on the ground that they must keep it because their neighbors do, and because there is an active demand for it by jobbers and retail dealers.

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VOL. III. No. 6.

AN
EPHEMERIS
OF
MATERIA MEDICA, PHARMACY,
THERAPEUTICS
AND
COLLATERAL INFORMATION.

APRIL, 1892.

BY
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CHARLES F. SQUIBB, A. B.

BROOKLYN, N. Y.
1892.

NOTICE.

These pamphlets have always been issued without charge, and although they were sent out for a few years with fair regularity, they are now very irregular and infrequent, and may at any time cease altogether. No one need write to know why he does not receive them more regularly or more frequently, because if he has not changed his address, all will have been sent to him, and much time is required to answer such letters.

A list is kept with care of all who are supposed to be specially interested in Materia Medica and Pharmacy, and however irregularly and infrequently these pamphlets are published, one copy of each issue is mailed without charge to each name on the list, and the list is, as it has always been, freely open to new names that may desire to be upon it.

But after an issue has been distributed, neither copies of that nor any other back issue can be sent free of cost, and all orders, to receive any attention, must be accompanied by ten cents in postage stamps or postal note for each pamphlet wanted.

The two completed volumes, separately bound in cloth, are still accessible to any who may want them and will remit $1.16 for each or for either volume. On receipt of the money they will be mailed postage paid.

This number completes Volume III., and by June 1st that volume will also be bound, and may be had by remitting $1.16.

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AN EPHEMERIS

OF

MATERIA MEDICA, PHARMACY, THERAPEUTICS AND COLLATERAL INFORMATION.

VOL. III. APRIL, 1892. No. 6

BRIEF COMMENTS ON THE MATERIA MEDICA, PHARMACY, AND THERAPEUTICS OF THE YEAR ENDING OCTOBER 1, 1891.*

ALPHABETICALLY ARRANGED.

In the following brief commentary, the aim has been to give a short, compact digest of the prominent current literature of the professions of pharmacy and medicine. There has been no attempt at treating the subject exhaustively, in the way of noticing everything that has been spoken of in relation to these allied topics ; but an effort has been made to sift the great accumulation of matter presented during the year, and give what may be of some little service to those seeking for general information as to how matters are progressing in the line in which a busy practitioner is supposed to be interested, and yet is unable to give the time to even hurriedly skim over the literature in order to keep abreast of the times.

The alphabetical arrangement is intended, of course, to aid in easy reference to any individual article as it comes up from time to time.

Abstracts were introduced into the U. S. Pharmacopœia of 1880 with a considerable expectation that a need was felt by the medical and pharmaceutical professions for just such a class of preparations. Up to this time the need has not been evident, and it might be well to consider the advisability of striking them from our official list.

Acacia, or true gum Arabic, is becoming scarcer every year, and it is now being both adulterated and substituted by gum

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*Read by title at the Eighth Annual Meeting of the New York State Medical Association, on October 30, 1891, by E. H. Squibb, M. D.

Senegal—an inferior grade. It is worthy of note that just at this time, and doubtless due to the scarcity of the true gum, close investigations are being made of wattle gum, obtained from several species of the Australian acacia. We may, therefore, probably look to this quarter to at least partially supply the deficiency.

Acetanilid (antifebrin) has lost much of late of its vaunted reputation on account of its impurity. Toxic effects have been unexpectedly produced from even fairly moderate doses, although prescribers seem to differ very considerably in what they consider the proper dose. Its apparently marked antipyretic properties, with which it started out, are less relied upon than formerly. Its good effects are to be found in its analgesic and hypnotic action. Its results have been harmful in some cases of typhoid fever, especially in pregnant and nursing women. Good results are to be looked for in neurotic affections, such as lumbago, neuralgias, severe rheumatic pains, sciatica, and the like. However, it appears to be safe and useful as a hypnotic in children, especially when affected with bronchitis or croupous pneumonia. Its comparative insolubility, and thus tastelessness, together with the smallness of dose, recommend it strongly in these cases. It may be well administered by placing the drug itself, or mixed with a little sugar, well back on the tongue, rather than attempt to improvise some mixture. Nothwithstanding conflicting results, this article has come to stay, and has recently been added to the British Pharmacopœia. No doubt the revisors of our own Pharmacopœia now at work will also give it attention.

Acid Agaricic is a new resin-acid, which has not made much of a reputation yet. It is obtained from the fungus *Polyporus officinalis* growing on larch trees, and is seen in small white crystals. It has been used with some effect in phthisis for checking the night-sweats while diminishing the thirst and excretion of urine. It is somewhat cathartic in its action, but tends to lessen vomiting and purging. It is only slightly soluble in water.

Acid Camphoric is the product of the oxidation of camphor by boiling with nitric acid, and occurs in small, white, odorless crystals It is insoluble in water, but readily soluble in alcohol. It is absolutely tasteless, and free from that burning sensation so characteristic of camphor. It was first used by Reichert, in 1888, in acute and chronic affections of the respiratory organs, in angina, coryza, and the like. Afterwards Fürbringer used 2 per cent. injections in cystitis, and recommended it against the night-sweats of consumptives. This latter recommendation was put in practice with markedly beneficial results. Schultze has met with good results, and suggests the use of antipyrine in the usual quantity in conjunction with the acid, to counteract the diaphoresis. Combemale has also published his gratifying results. Dr. Hare, of Philadelphia, now most heartily endorses Combemale's good results, as he had used it with great satisfaction in ten consecutive cases. It surely deserves more extended trial, not only in the night-sweats of phthisis, but in the profuse sweating from other causes.

Acid Carbolic is still subject to the same reddening that has occurred in past years; and although emphasis has been laid on the fact that the reddening has not altered its medicinal efficiency, still the white crystals are sought after by preference, and some even go so far as to refuse the colored as unfit for use. The recent production of the synthetic acid has not helped the matter, as it also is subject to the same change. This latter observation more than any other led observers to look for the cause as being extrinsic rather than intrinsic. E. Fabini conducted a series of careful experiments to this end, and now believes he has discovered that the reddening is due to contact with copper vessels, while the acid has combined with ammonium. We have long recognized the reddening effect which ammonia vapors would produce, but had not suspected that a metal was necessary as well at the same time. Fabini's deductions are not necessarily conclusive, but they are interesting and instructive as being a step in advance.

The remedy suggested—to avoid contact with metals from beginning to end—would have rather a prohibitive restriction to its manufacture, if it is desired to produce it at a reasonable figure for general use.

Chromic Acid has been much improved in quality and uniformity, and no doubt there will now be no more trouble in getting it regularly of the fine quality we now see it. This is all of foreign manufacture, and surpasses anything ever produced here. The chief objection in times gone by was the lack of care in washing it free from sulphuric acid. When the surgeon is looking for the caustic effect of this acid, he does not desire to see that of sulphuric acid developed as well.

Acid Cresotic, as used in medicine, is strictly the *para*cresotic acid, for there are three modifications,—the *ortho,* the *meta,* and the *para* acid. Mr. H. Helbing, of England, has recently shown very clearly that this acid bears the same relation to cresol that salicylic acid does to phenol, and it is prepared in the very same way that Kolbe prepared salicylic acid synthetically. The sodium salt is the one usually used in medicine, and is called in full *paracresotate of sodium.* The doses and uses are the same as those of salicylate of sodium. The results claimed for it are better than those obtained with salicylate of sodium, but it has been little used in this country as yet. In England it has been in use for some time, and Prof. T. R. Fraser, of Edinburgh, has an accumulation of cases giving very encouraging results, which he proposes to publish shortly.

Acid Hydrocyanic Diluted, as prepared by the official process, is still prone to early decomposition. Many experiments have been repeated to remedy this defect, without improvement. Preservatives have been added, and various solvents have been used to hold the gas, but nothing has succeeded any better than distilled water. Extra precautions in the manufacture and in observing cleanliness in the retaining packages give moderately good results, but nothing very definite has been accomplished yet.

Acid Oxynaphthoic is of recent introduction into medicine. It is a naphthol product, prepared in a roundabout way, which is not of moment here. It occurs as a white powder, devoid of odor, and therefore will be in this respect a strong rival of iodoform, as their uses are alike. It has been used in several skin affections with gratifying results. It is said to be five times stronger than salicylic acid in its antiseptic effects. It is not used internally, but has been employed in solutions of 1 to 100 with phosphate of sodium for vaginal injections. Meagre reports only are yet at hand.

Acid Salicylic, as made artificially, has during the past year undergone a considerable amount of investigation and discussion, principally in Great Britain. It has long been noticed that at times a marked depressing effect followed its administration, and to determine the cause has been the reason for critical examination. The pharmaceutical chemists are apparently at variance on the matter, as the cause had been stated by some to be cresotic acid, and particularly paracresotic acid. This conclusion has been received very skeptically in many quarters since the paracresotate of sodium has been used medicinally with such gratifying results in cases where salicylate of sodium had previously been used unsuccessfully. However this may be, some foreign substance evidently does exist in the English acid which it is aimed to avoid, and investigations are still in progress. Practically all that is used in this country is of German make. Although there are several grades of this acid sold by the Germans, still the grade that is sent here is for the most part the best, and we get very little of the bad effects which our English brethren notice.

Acid Salicyl-sulphonic (sulpho-salicylic acid) has again been brought to notice as a test for albumin, although it has been known since 1889, when G. Roch first called attention to it. Dr. John A. Macwilliam, of the University of Aberdeen, elaborates the subject in a manner which invites attention.* This acid is obtained by the action of sulphuric anhydride on salicylic acid, or by heating salicylic acid with strong sulphuric acid, and occurs as colorless, needle-like crystals, freely soluble in water.

Acid Trichloracetic offers us another great agent for detecting albumin in urine. It is one of the newer tests, which bids fair to remain with us. It has been used considerably since it was first brought forward, and with success. Insurance examiners are the loudest in praising it. It may be used in the form of a saturated solution, or a crystal of the acid may be dropped in the suspected urine. The turbid line, which forms immediately at the junction of the liquids, is to be distinguished from that formed by urates by the rapidity of formation of the former.

This acid has also been found effectual as a caustic and astringent. In throat and nose affections its effect is much more local than some of the other caustics. It is readily soluble in water, and deliquesces easily. Out of 140 cases treated by one practitioner, 87 needed but one application. Dr. J. W. Gleitzmann of this Association has met with very favorable results, and summarizes as follows : "1. Trichloracetic acid compares favorably with other caustics in hypertrophic conditions of the throat and nose, and is a valuable addition to the remedies now in use. 2. In the greatest majority of cases it is sufficient to produce the desired reduction of tissue, although it does not supersede the galvano-cautery. 3. It can be applied with safety to the larynx without any evil consequences. 4. Its chief advantage in nasal affections is the dryness of its eschar, which prevents unpleasant sequelae, and makes after-treatment unnecessary.†

Alkaloids are now a class of preparations greatly on the increase. Physicians continue to demand of the manufacturer that his medicaments be condensed into the smallest space, and offered in the most convenient and accurate form for dosing. This has led the manufacturer to attempt to isolate every active principle possible, and discard the old-fashioned preparations. It is now coming to pass that physicians are not obtaining the results they looked for in many cases of the apparently isolated alkaloids, because they have expected the same effects from these that they used to get from the officinal preparations of the drugs themselves. It is time, then, to call attention again to the oft-repeated fact that the individual effects of such alkaloids must alone be looked for, and not the general effects of the drugs, which latter effects, in many cases, are the ones expected. Again, the alkaloids apparently isolated are at times suspected of being either wholly or partly the product of the chemical treatment, and may not necessarily exist as such in the drugs beforehand. The accuracy of our chemical knowledge, especially in regard to organic chemistry, is not by any means definite enough for us to state positively that the final result of our chemical treatment of a drug existed there before our manipulation. Thus it follows that the therapeutic effect of the apparently isolated alkaloid may be quite different from its effect in the initial preparation of the drug just previous to our manipulation of it.

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* Brit. Med. Jour., April 18, 1891, page 837.

† Med. Record, vol. 39, page 312.

Amylene Hydrate (tertiary amyl alcohol) is a colorless, oily liquid of a camphor-peppermint odor, prepared by the action of diluted sulphuric acid on amylene, and distilled. It was introduced some years ago as a hypnotic, and was then found to be safe, and superior to paraldehyde, as it produced no disagreeable after-effects. It is not, however, equal therapeutically to chloral. It is found now to be not only hypnotic, but anodyne, in its effects in some cases. It apparently does not disturb the respiration or heart's action. It appears to act successfully in cases of nervous sleeplessness, especially in children suffering from whooping cough. Epilepsy has been well treated with it; and if it appears to be too weak in its action, a little morphia added in conjunction improves its beneficial effects. It deserves further trial.

Anæsthesin, synthetically prepared, was exhibited at the last International Medical Congress in Berlin. Messrs. Gehe & Co. since then claim this to be bromacetanilid. It was a white, crystalline powder offered as a rival to cocaine in local anæsthesia. Little has been heard from it or about it since that time, and therefore we have little professional interest in it as yet.

Antikamnia, the new "analgesic, antipyretic, and anodyne," which was so suddenly and attractively thrust upon us, proves now, upon careful analysis, to be nothing more than a mechanical mixture of acetanilid and commercial bicarbonate of sodium rubbed up into a fine powder. Its therapeutic effects have been good, but only to the same extent as acetanilid itself, with the noticeable advantage, however, of acting more quickly and in smaller doses, due no doubt to the presence of the bicarbonate of sodium. Under the above circumstances, then, it would be far better to extemporize a prescription of about 75 per cent. of acetanilid, and pay about one-tenth the price the leading firm exacts.

Antinervin was introduced into medicine a couple of years ago as being analytically salicylbromanilid, and similar in its effects to acetanilid, with its accompanying disadvantages. Its recommended efficiency in diabetes has not been verified, and we hear little of it professionally. It may be of interest, however, to learn that, from a careful examination, it is now concluded to consist of a mixture of 50 parts acetanilid, 25 parts salicylic acid, and 25 parts of bromide of ammonium.

Antipyrin has lost very little of its popularity during the past year, but the profession has been gradually learning to use it with caution. Several very trying poisoning cases, with some deaths, have occurred from its use, even after moderate doses; but the larger proportion undoubtedly were not entirely due to the antipyrin. It has surely come to be considered now as one of our useful therapeutic agents, and it has been recently added to the British Pharmacopœia under the name Phenazonum (Phenazone). It is becoming more and more recognized as an analgesic, and its antipyretic properties are rather confined, in the hands of careful observers, to cases of hyperpyrexia. Its marked advantage over many of its rivals is its ready solubility. The profession appears still to be divided as to whether its best effects are produced from small repeated doses, or from large infrequent ones. Some lately have claimed that it is almost a specific in puerperal fever. Its successful use as an antigalactic is markedly on the increase, and care is constantly recommended in administering it to nursing women. It has quite a reputation at the present time in whooping cough and incontinence of urine in children. M. Gundez treated 37 cases of incontinence, with 19 cures and only 3 complete failures. M. Périer emphasizes—what many others have noted—its decided beneficial effects as a hæmostatic in minor surgical operations. The dermatologists have sounded its praises, both in this and the old country. Blaschko read a paper before the Berlin Dermatological Society, stating that he believed the most marked results were obtained in those skin affections accompanied by pruritus. Much attention has been given within the past year to its use in diabetes mellitus, and quite an array of statistics are now availabile both in our own country and abroad. The French, in particular, give very favorable opinions of this use of it in such selected cases where polyuria is prominent and in elderly persons. Its principal abuse is met with in its general popular use for headaches and minor ailments. Very little attention is paid by the laity to the direct cause of a headache. The immediate attention is given to getting rid of the pain, rather than to seeking the cause in some form of indigestion or rather minor indiscretion, and applying a rational treatment of the economy as a remedy in place of medication.

Antipyrin has shown itself capable of combining with other substances to form new products for which investigators claim therapeutic value—forming hypnal, salipyrin, resopyrin, and others formed with the phenols. M. Patein, of the Paris Society of Pharmacy, maintains, however, that these new compounds can rationally have no therapeutic value as compounds, on account of their immediate decomposition upon contact with the digestive secretions.

The use recently of the double valerianate of antipyrin and quinine in neuralgia has given considerable satisfaction.

Antiseptol (cinchonine iodosulphate) represents one of the various recent attempts to obtain an efficient substitute for iodoform without the objectionable features of the latter. It is odorless, and is made by the addition of a solution of iodine and iodide of potassium to sulphate of cinchonine. Its use is largely confined to continental Europe, and little is heard of it as yet in Great Britain or in this country.

Aristol is one of the new antiseptics brought forth as a substitute for iodoform. It is a reddish-brown powder obtained by treating a strongly alkaline solution of thymol with iodine. It gradually becomes paler in color, due to the iodine given off from exposure to sunlight and to heat. It therefore should be kept from an undue amount of light or heat. It has the disadvantage in some respects of being insoluble in water. Owing to its unstable nature, the excipients which may be employed are limited. It is used mostly in the powdered form, but its use with olive oil, collodion, and the ointments in general is rapidly on the increase. For the two previous years it has been mostly known by the name of "annidalin," but recently, and since the inauguration of new modes of preparation, it has been urged forward with renewed vigor under its present name.

From recent investigation it appears that its efficiency is largely due to its instability, and any attempt to render it free from its property of slowly giving off iodine renders it comparatively inert. It has been suggested that this very fact may account for some of the failures which have been reported by some investigators.

Aristol at the present time has universal testimony as to its usefulness in medicine. Some go so far as to claim that it is one of the most important additions to our materia medica in recent years. Its antiseptic power is very pronounced. It has a slight, but not unpleasant, odor. When dusted on open wounds or ulcers it is not irritant, and promotes rapid cicatrization. It has no toxic effects, as iodine cannot be found in the urine after using in any of its forms of application. It is, therefore, a safe remedy to leave in the hands of the patient, as experience has now proved. None of the iodoform substitutes have as large a proportion of iodine as iodoform itself, aristol having less than one half. It has now been employed wherever iodoform had been, and with very gratifying results almost universally. In some quarters discouraging results have been obtained in syphilis, but better ones in venereal ulcers, the complaint being its slowness of action and its inferiority to iodoform in therapeutic activity. Good results are reported on all sides in diseases of women, particularly in endometritis, cervical erosions, vulvar eczema, and cancer of the cervix—acting as a most effective disinfectant and deodorizer. From continental practitioners come good results in several cases of ozaena, giving in one case better satisfaction than iodoform just previously tried. In naso-pharyngeal catarrhs in combination with petrolatum it has been sprayed on the affected parts with good effect. In psoriasis it seems in general to give satisfaction, but is not so prompt in action as chrysarobin. Its other advantages, however, make it a formidable rival Dentists have now found use for it in the treatment of ulcerations and in disinfecting cavities. It noticeably arrests pus formation. The fine powder has been dusted on the vesicles in poisoning by poison oak, giving much relief, and reducing the burning and swelling of the parts. No record is yet found of its having been used in preventing the ulceration and pitting of variola.

Benzoyl Eugenol (benzeugenol) is a new product without any history in a therapeutical way; but if expectations are realized, it aims to be a valuable remedy in tuberculosis. It is made by a patented process from the union of the principal constituent of oil of cloves, called eugenol, with benzoyl. Oil of cloves itself has been used in the treatment of this affection before, and Dr. Koch has suggested the internal administration of eugenol in tuberculous patients. Investigators in Berlin then took up the production of this compound. It is seen in colorless and odorless needle like crystals, of slightly bitter taste, practically insoluble in water. Nothing at all has been heard of it medicinally in this country, and the accounts from the old country are still very meagre.

Betol (salinaphthol) is a compound of salicylic acid and naphthol, very similar to salol, and applicable to the same uses. It was expected theoretically that this new compound would be superior in action to salol; but clinical experience has not been generally favorable, although good results are reported from its use so far as an intestinal antiseptic. It comes as small, colorless, and odorless broken crystals insoluble in water. Its taste is not disagreeable, and its toxic effects are not noticeable in moderate doses. It is, therefore, a reasonably safe remedy in children's bowel complaints.

Bromoform still continues to give satisfaction in the treatment of whooping-cough, although its use has apparently been confined to only a few observers. Care must be taken to see that it is in normal condition, that of a colorless liquid, for by exposure to the light bromine is set free and colors the liquid. Foreign observers are most pronounced in its favor, and more practitioners in our own country should put investigations on record.

Bromol (tribromophenol) is not new, but has been known as the product of the action of bromine in excess on carbolic acid. As it has been found now to have marked antiseptic properties, this short name has been given it, both for convenience in use and to be in harmony with the already too many new compounds being pushed forth, most of which have names less indicative of their true composition. It has been applied with vaseline to open wounds with success. Its internal uses have been in cases of typhoid fever and cholera infantum. Little has been written yet on its therapeutic uses.

Cactina is the proximate principle of the night-blooming cereus, and has been found by Dr. O. M. Myers to be a valuable cardiac stimulant. His results are very gratifying, and go to show that it has less disturbing effects on the stomach than digitalis. His observations deserve attention.* Observations of others are not on record.

Camphor in the form of camphorated oil (1 to 10) has been given a share of the universal attention paid to phthisical patients during the year past. Good results have followed from its hypodermic injection by practitioners in Berlin. It has been tried in most pulmonary affections, and in bronchitis, tonsilitis, and coryza with some satisfaction. Nothing of note is mentioned from this country.

Cannabis Indica has fallen considerably in the estimation of the profession, both in the old country and in this, due no doubt to its variability and often noticeable uncertainty of action. However true the cause may be, there is no doubt that an almost extreme limit has been reached, and the profession needs to be reminded anew of the marked value of the drug in many cases. Attention is therefore here called to the very favorable report of Dr. C. W. Suckling, M. R. C. P., as given in the *British Medical Journal.** He calls attention to its value in a form of insanity described by him, in the treatment of melancholia and mania, in chorea when arsenic has failed, in migraine, as a gastric sedative, and as a hypnotic—its value being well established in the treatment of all cases met with in insane asylums. It deserves more attention than the profession has given it of late.

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* N. Y. Med. Jour., vol. liii. page 681.

Cantharidin, in the form of cantharidinate of potassium or sodium, has been brought forward by Prof. Oscar Liebreich, of Berlin, as an effective remedy in tuberculous affections, principally lupus and laryngeal phthisis. Dr. Wolfert, of Berlin, has called attention to the interesting fact, that as long ago as twenty years, Russian peasants habitually employed a species of beetle in cases of cancer. It was early noticed that this principle, cantharidin, exhibited the remarkable property of exciting exudation from the capillaries. This led Dr. Liebreich to select it as he now recommends. He uses the potassium salt hypodermically, and states that the sodium salt is much milder in action. His experience, and that of several well-known co-workers, show that markedly beneficial results may be expected in diminishing the destruction of tissue common to tuberculous affections. Dr. Gerhardt, however, is reported as having used Liebreich's treatment in twenty cases with unfavorable results. It is to be particularly noted that the German observers seem to be convinced that slighter disturbance is produced with cantharidin than with the tuberculin of Koch. Surely more extended clinical experience is much needed, and it is to be hoped that some other cases than hospital ones will be reported more generally by our own countrymen.

Chloralamid (chloral-formamide) is the new hypnotic obtained by the combination of chloral and the colorless, oily, liquid formamide—an organic compound allied to urea. Our foreign brethren are very enthusiastic over their results with it as a decided rival to chloral and sulphonal. Its best effects are produced in cases of idiopathic insomnia, cases where the insomnia is not due to either extreme pain or excitement. Although it may succeed in some cases in overcoming slight pains, it cannot be classed as an anodyne. It induces a natural and refreshing sleep, and, as a rule, is not followed by headache on waking the following morning. A sense of well-being is the result of the rest it affords. It is thought by some to be a deeper sleep than that produced by chloral. There have been some failures to produce sleep with it, but the per cent. of such cases is small. Some Parisian and German observers claim that its action is exactly the same as chloral hydrate, if allowance be made for the smaller proportion of chloral anhydride in the chloralamid. It was supposed that it acted by decomposing in the circulation, liberating chloral; but there does not occur with it the marked depression so characteristic of chloral. In the majority of cases it works well, but in a small proportion there are unusual effects, not, however, in greater proportion than with morphia or chloral. There are no apparent cumulative effects, and no craving for it is noticed, although it may be given nearly every twenty-four hours for several weeks. Of late some success has been met in cases of epilepsy; but the most satisfactory results have been obtained in senile insomnia, pulmonary diseases, and hysteria. It appears to possess the very happy property of counteracting the desire to micturate at night in senile cases. It occurs in colorless crystals, with a mild, slightly bitter taste, and without odor. It is soluble in about ten parts of cold water, and one should be cautious not to dissolve it in warm water, nor to heat the solution after it is made, as it very readily decomposes. Its use in this country is rapidly spreading.

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* Vol. ii., for 1891, page 12.

Chloralimide was first described by Pinner and Fuchs, who obtained it by the action of ammonium acetate upon chloral hydrate; but it is now claimed that it can be obtained in a state of greater purity by a more approved process. It occurs in long, colorless, needle-like crystals, without taste or odor. It is only slightly soluble in water, and is very stable in its composition, not being altered by air, light, or moisture, nor by heating up to 179°C. At 180°C., however, it is decomposed, yielding chloroform and formamide. It is classed by its introducers as a superior hypnotic to chloralamid, and much stress is laid upon the very possible but culpable error the profession might fall into of prescribing the latter for the former, whereas it would look very pointedly to an outsider as if the rival adherents purposely chose such extremely similar names for their compounds that one might insidiously take advantage of the trade of the other. Little has been reported in a general way therapeutically upon the use of this agent.

Cocaine Phenate is a new salt formed by the combination of phenol with cocaine. Knowing the similar effects of these two ingredients, the aim of the introducer has been to substitute an acid element having some expected beneficial effect for the commonly used hydrochloric acid, which had little therapeutic effect, if any, and served no purpose other than to present the alkaloid cocaine in a soluble form. This new salt has now had a trial of about a year, and satisfactory results are reported from Germany. It has been employed in nearly every shape and in nearly every affection in which the hydrochlorate has been successful. No results of any extent have as yet been reported of its use in this country.

Creasote has met with very gratifying success in the treatment of phthisis during the past year. The profession seems to be quite unanimous in its approval of this remedy. It should be emphasized, however, that the beechwood creasote is the reliable article, as vouched for by the medical profession of both continents.

Creolin is one of the. now very numerous products of the destructive distillation of coal tar. It is a very complex body, being a mixture of several of the coal-tar products, of the consistency of syrup, and of a brownish-black color. It makes with water a milky emulsion, which becomes sticky after standing. It is said to have now proved itself a more powerful germicide than carbolic acid. The well established value of the products of coal tar in many forms of eczema and psoriasis, and the cheapness of this particular product, led dermatologists eagerly to apply it in their specialty. A wash of the strength of about 1 ʒ to 8 f ℥. of water seems to have been about the favorite solution for skin affections. Dr. Rothe, of England, has used a 5 per cent. ointment in erysipelas, eczema, and scabies, and is of the opinion that creolin forms a specific for the latter, being superior to sulphur in not producing an eczema of the skin and in not staining the linen. Several successful cases are now on record when used as an enema for typhoid diarrhœa in a solution of 1 ʒ to 16 f ℥. of water. A Brazilian practitioner reports having used successfully an application of a 1 to 2 per cent. solution for soft chancres. He claims that it acted more rapidly in some cases than either iodoform or corrosive sublimate. German observers have used a 1 per cent. solution in purulent ophthalmia neonatorum with varied success. Cases of thrush and aphtha have been cured, however, by washing out the mouth and pharynx with this strength of solution. As many as 2,000 midwifery vaginal injections have now been made at

Breslau with very encouraging results. Creolin appears to have no special hæmostatic action. In dental practice this article has become quite a favorite, and is used in a weak solution as a mouth wash, in treating suppurating surfaces, and as an effectual deodorizer of a dead cavity. In some cases among its varied uses, and especially in children, toxic effects are noticed, the urine showing the presence of phenol. A 1½ per cent. solution has been known to have produced marked toxic effects.

Cresalols (cresol salicylates) are crystalline compounds analogous to betol and salol. By heating molecular equivalents of salicylate of sodium, cresylate of sodium, and phosphoric chloride, one of three cresalols (ortho, meta, or para) is formed, depending on the sodium salt used. All three forms are bulky white powders, with an odor like salol, and insoluble in water. They are recommended to be used as antiseptic dusting powders. Being without disagreeable odor, they are preferable to iodoform, and it is claimed that they lessen more effectively the secretions from wounds. Nencki believes para-cresalol to be superior to salol for producing asepis in the intestinal tract. Not much has been heard of these as yet in a general way.

Dermatol is the patented name given to the basic gallate of bismuth, introduced as an effective substitute for iodoform. It is made simply by bringing together bismuth subnitrate and gallic acid under proper conditions to form the new salt. It is described as a fine saffron-yellow odorless powder, insoluble in the ordinary solvents. By reason of this insolubility its antibacterial action is confined to the immediate locality of application, and thus it comes in direct contact with the microbes there present, as iodoform is supposed to do. It is claimed that it has a desiccating effect as well, by which it dries up the aliment of the bacteria. Its astringent property is said to promote the healing process, and yet does not cause irritation, and is not absorbed. It is stated to be of value when given internally in gastric and intestinal affections. It does not appear to be poisonous in quite large doses. It has been used in the form of ointments, suppositories, emulsions, and by insufflation. A gauze impregnated with it has been of service.* To avoid countenancing a patented article when it can be so easily accomplished, the profession would do well to prescribe bismuth gallate simply.

Diuretin (sodio-theobromine salicylate) is the name given to the double salicylate of sodium and theobromine. It is a white powder, readily soluble in water, but very unstable. It is easily decomposed by acids, and even exposure to the carbonic acid found in the air will be sufficient to break down the compound. It has been used principally in the old country, with increasing frequency since its introduction somewhat over a year ago. Its price is high, and this has been one of the reasons for its limited use in this country. The general results have been various, and some would doubt its usefulness. It is said to rival caffeine and digitalis in its having no action on the heart or nervous system. It is readily absorbed and markedly diuretic. As it would readily be decomposed in the stomach, one investigator claims that it does little good unless it be administered in some form which may pass the stomach unacted upon. It may be considered not only as a diuretic, markedly beneficial in cases of dropsy, but also as a cardiac remedy, especially in cases where disturbance of the circulation depending on valvular incompetence is present. In acute nephritis much greater diuresis occurs than in the chronic form. The quantity of albumin is not altered. In one patient with cirrhosis of the liver, no diuretic action was noticed. In a healthy man the amount of urine passed is greater. It was mentioned by Dr. C. Gram, of Copenhagen, in his original article, that the diuresis resulted from the theobromine in the compound, and that the sodium salicylate had no effect. Others doubt this conclusion, as accumulated observations go to show that sodium salicylate and salicylic acid both act diuretically to a marked degree. There appears to be some danger at times in cases of copious diuresis that the ascites and œdema may disappear so rapidly that collapse may occur. Foreign observers strongly advise more extended trial.

Ether versus **Chloroform** is the form of the important and animated discussion to which our English brethren have given a good share of the attention which has not been given to the subjects of Koch's "tuberculin," la grippe epidemic, and the report of the Hyderabad Chloroform Commission. The conclusions arrived at by this commission were by no means satisfactory to a large part of the profession, and other investigations were started and completed during the year with conflicting conclusions. The English are surely partial to chloroform; and when recently the number of deaths under and following its administration were reported largely on the increase, it put the enthusiasts and the manufacturers on the defensive to explain the cause. The purity of the chloroform was, of course, loudly questioned; but by careful testing it was proved that the fault must lie elsewhere. The most conservative explanations given were, carelessness in administration and idiosyncrasy of the patients. Although a strong, but small, proportion of the English profession, and a very much larger proportion in our own country, confidently believe, both from experimentation on animals and from actual clinical practice, that ether is the safer and superior anæsthetic, still sectional teaching and actual long practice in the various sections confirm one's faith in the one he has been taught to use and has always used. The English, for example, are evidently wedded to the use of chloroform, and have been ever since its discovery. In our own country the sectional feeling is quite interesting, but apparently unexplainable, except in some such way as stated above. In the Eastern States we might almost say that ether alone is used. To be sure it is the home of ether; but ever since its introduction the teachings of the medical schools and the practitioners generally have been to anæsthetize with ether as a matter of routine. Again, in our Southern States, or, rather, south of Maryland, Pennsylvania and the Ohio river, the profession, on the other hand, make use of chloroform as the routine practice. They are not as exclusive as the New Englanders on their side, but the preference is quite marked. At this stage of our progress, then, we, as a profession, throughout the civilized world, are quite divided in our preference for these two anæsthetics.

Ethyl Bromide (hydrobromic ether) continues to be used as an anæsthetic in minor surgical operations, but is most largely employed in dental practice. Owing to its very unstable nature, a word of caution again may not be out of place. Many fatal cases have been reported during the year, and its history from the very beginning has been marred by these constant unfortunate results. Even after following all the ordinary precautions as to using the *whole* of the contents of a purchased package at one operation, and as to avoiding exposure to light and air, apparently unexplainable and bad results follow in many cases. When it does act properly, it is such an attractive anæsthetic in its immediate effects and agreeable after-effects that the operator is strongly tempted to resort to it again and again, until, by some unfortunate carelessness or impurity, he has finally to record, like others before him, his fatal case.

Ethylene Bromide is a new sedative introduced to avoid the undesirable symptoms often noticed from the effects of the alkalies (potassium and sodium) usually used as the bases in the salts administered. It is a heavy, clear liquid, of a brownish tinge, with a taste at first sweet and afterwards giving a burning sensation, and with an odor much like chloroform. It is obtained by conducting olefiant gas into bromine at a low temperature. It has been used somewhat largely in the old country, in cases of epilepsy in both the young and old, with good effect, but is little known to us here as yet. It contains by weight 87 per cent. of bromine, and to this its action in epilepsy is attributed. It is insoluble in water. Care should be taken in prescribing not to confuse this with ethyl bromide last spoken of, as the difference in name is very slight when either pronounced or written. Fatal cases are already on record from confusing the two.

Euphorin is the somewhat trivial name given in the past year to the synthetic compound phenylurethane discovered and introduced in the year previous by Prof. Giacosa, of Turin. It has quite recently been more in demand, and the profession in this country are using it more freely. It is one of the numerous anilin products occurring as a white crystalline powder, with a slight aromatic odor, and with very little taste of any kind at first, but becoming somewhat acrid and clove-like. It is only slightly soluble in cold water. Adler early recommended it on account of its slightly unpleasant after-effects and for the increased diaphoresis manifested. Neither phenol nor anilin occurs in the urine, and albumen and sugar are not met with, but probably the secretion of urea is increased. The analgesic effects claimed for it are variable. The cases of orchitis reported seemed to be the ones most relieved. Its antipyretic properties are supposed to be effected by the dilatation of the peripheral blood-vessels, and these were looked upon as the chief properties of the compound, for the new name signifies a sense of well-being and comfortable relief which is characteristic of its action in the stage of apyrexia after its administration. Dr. L. Sansoni has found it free from any objectionable action, such as occasionally follows the use of antipyrin, acetanilid, phenacetin, and sodium salicylate. It is stated to be equal to twice its weight of antipyrin. It is claimed to have pronounced antiseptic properties. Dr. Sansoni applied the powder to indolent ulcers and chronic cases of ophthalmia, and met with such encouraging results that he urges further trials by others. Its action here is explained by the setting free of phenol, the result of its splitting up when in contact with the secreting tissues. Its quick and sure action in these cases, with very little pain, is its great recommendation. During the year, Prof. Stiller has used it quite extensively in the Jewish hospital at Pesth, not with uniformly good results, but in the large majority of cases with marked success. His cases were those of supra-orbital neuralgia, sciatica, chronic nervous headache, rheumatic fever, chronic articular and muscular rheumatism, and in six cases of habitual hemicrania seen in private practice the results were remarkably successful. The doses employed were from three to six grains repeated from three to five times per day.

Europhen is the confusing name given to another of the now numerous substitutes for iodoform. Chemically it is isobutyl-ortho-cresol iodide, and is the product of the action of iodine upon a compound body of the phenol type. It is said to contain 27.6 per cent. of iodine, and is a yellow amorphous powder, with an aromatic odor recalling that of saffron. It is insoluble in water, and care must be taken when solutions are made in alcohol, ether, chloroform, etc., that they be made in the cold, as heat decomposes it, setting iodine free. When applied to dry surfaces it appears to be inert, and in general it acts only when in contact with secreting surfaces, where it is decomposed and iodine liberated slowly. Its advantages over iodoform are its freedom from disagreeable odor, and nontoxic effects, that it does not cake so easily, and is so light that a given weight will cover five times as much surface. It is especially applicable in venereal and syphilitic cases.

Exalgin (methylacetanilid) is the compound allied to acetanilid and introduced as an analgesic. It is not new by any means, as it was first described in 1874, and has now been before the profession for many years, but has only received meagre attention until very recent times. Even up to last year, as careful an observer as T. R. Fraser, of England, thought that although its analgesic power was not very great, still it might take a useful and important place among the remedies to relieve pain, on account of the freedom of its action from the disturbances accompanying the action of nearly all other pain-relieving agents. Dr. Sinclair Holden concludes that it is useless in alleviating pain due to mechanical or organic lesions. This would account often for its failure in apparently suitable cases where the cause is obscure. It has the advantage when given in small doses of being perfectly safe, and the general conservative opinion seems to be that the dose must be kept small, and repeated if necessary, as serious results have frequently followed overdosing. The affections in which it is of most marked service are the neuralgias, especially facial, anaemic, visceral and intercostal neuralgias, and also neuralgias of the various plexuses, and the ilio-lumbar pains due to uterine and ovarian disease. Angina pectoris, nephritic colic, and painful menstruation are greatly relieved by it. It should not be used popularly, but always under medical advice and direction.

Guaiacol is the liquid compound obtained by the fractional distillation of beechwood-tar creosote, and contains from 60 to 90 per cent. of creosote. It was years ago introduced as a substitute for creosote, and Prof. Sommerbrodt first used it in the treatment of phthisis. The literature of the subject is now pretty extensive, particularly in the old country, and tends to prove that it is decidedly beneficial in the early stages of the disease. In order to carry out the so-called intensive creosote treatment, it was necessary to get large quantities of guaiacol into the system, and thus the salt guaiacol-benzoate was introduced under the name benzoyl-guaiacol or benzosol. This compound permits of the administration of an amount of guaiacol which otherwise would be almost impossible owing to its caustic properties. The results with this have been varied, but on the whole they should invite further trial. Guaiacol salicylate also has been introduced under the name guaiacol salol as an intestinal disinfectant. From Bovet's experiments it would appear that it splits up into its two parts of base and acid in the intestinal track. Quite recently Dr. W. H. Gregg, of our own country, has reported* on the administration of the iodide by the intestines in the treatment of tuberculous disease of the lungs. He believes it to be the most active therapeutic agent we possess for this treatment, but it must be taken in large quantities. He says we need not hesitate to give by this method thirty to fifty grains without fear of overdosing, since it does not become poisonous until one hundred grains have been absorbed. The administration by enema is a simple and practical method, and one to which the patients do not object. The results are certainly remarkable, and deserve confirmatory testimony. Apparently one dose in twenty-four hours is sufficient.

Hypnal (monochloral-antipyrin), the hypnotic compound obtained by dissolving about equal parts of chloral hydrate and antipyrin in water, has continued in use since its introduction with somewhat varied success. In the beginning, L. Reuter claimed that it was therapeutically inert; Dr. Bardet, however, early considered it an antispasmodic as well as a hypnotic. The general opinion now appears to accept it as chiefly hypnotic, although Dujardin-Beaumetz and Fränkel give it analgesic properties as well. The construction of the compound would of itself lead us to at once reason that it would be a useful remedy, as chloral in ordinary doses has little effect on pain, while antipyrin rarely produces sleep in relieving pain. It will, no doubt, receive much more attention by the profession during the coming year.

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* N. Y. Medical Journal, vol. liv., page 347.

Ichthyol (ammonium ichthyol sulphonate) obtained from the dry distillation of a bituminous quartz found in the Tyrol, containing fossil fish remains in great quantities, has, for some time back, been largely prescribed for external use but it has only recently begun to find favor as an internal remedy. Its peculiar and unpleasant odor is greatly against it, and necessitates its being given in capsules, or otherwise disguising it. About ten per cent. of oil of citronella has been used to accomplish this end, and proves of additional service in rheumatic cases, as it alone has been so used with good effect. Its external use has been further pushed during the past year with somewhat varied success. Dr. T. Cranston Charles very recently reports having used it with success in many different ailments where external application is called for. Dr. Freund speaks highly of it as an analgesic and antiseptic in the treatment of endometritis, and the literature in its favor in this connection is now quite voluminous. Köster makes good use of a one per cent. solution in gonorrhœa. Its antiseptic property is unquestioned. When given internally in conjunction with the external use, it improves the digestion and appetite, and makes a decided gain in the general health. Stocquart records favorable clinical results in using it to relieve the vertigo due to simple dyspepsia or indigestion.

Iodoform seems to hold on tenaciously to its claim for recognition, notwithstanding the now formidable and still increasing array of substitutes. The odor of course is the great drawback to its wide and more general use without disagreeable complaints. A few of the means to mask its odor may be here recorded. W. Pagenkopf recommends the addition of a small quantity of Russian turpentine oil, which would impart a peculiar and pleasant odor. Klingmann adds one part of iodoform to six parts of olive oil, and shakes for twelve hours before filtering off the clear saturated oil containing about three per cent. of iodoform. Dr. Ludwig Váczi prescribes an ointment of one part of creolin, two of iodoform, and twenty-five of vaseline. On allowing this to stand over-night the iodoform odor will have disappeared, and only a slight smell of creolin will remain. He says it will be found that the creolin not only does not irritate, but is also itself a good disinfectant.

Iodophenin is a new compound obtained by the action of iodine on phenacetin under certain definite conditions. It was introduced by Scholvien of Berlin as a powerful bactericide. It has a crystalline form, a heavy odor like iodine, an acrid burning taste, and is practically insoluble in water. It is said to act promptly in as weak a solution as 1 to 5,000. Besides its bactericidal property, it is said to possess antiseptic and febrifuge properties as well. It is at present under trial by our foreign brethren. Nothing has been heard from it here as yet.

Lysol is the name given to a saponified product of coal-tar, chiefly composed of the cresols, and is liquid in form. It is one of the very newest antiseptics. The reports are yet meagre, and they come wholly from the other side of the Atlantic. It appears to be superior to all the other antiseptics, according to the reports. One of its important features is, that it makes a perfect solution in water. Michelsen says that after a little trial he found he could use it effectually wherever carbolic acid, iodoform, or corrosive sublimate was used. The dermatologists have used it mostly, so far, and with varied results. The most recent clinical report comes from Dr. Leslie Phillips, of Birmingham, England, who used it in the treatment of lupus. He says it is surely worthy of extended use in the treatment of this disease, for a short period of treatment by it is sufficient to produce a decided improvement in the appearance of the disease, and the results are so pronounced as to suggest a permanency, the reality of which can only be determined, of course, after some time has elapsed.

Menthol (peppermint camphor), ever since its introduction into our materia medica as a remedy for neuralgia, has gradually expanded its general usefulness. The English have recently added it to their pharmacopœia. Its use in neuralgias has become very general, and although its effect often is only temporary, still in some of the milder facial neuralgias and rheumatic pains the relief is more lasting. Its use in the treatment of pruritus generally has greatly extended. Its antiseptic and anaesthetic properties have been markedly developed within the past year. Wolf's extended use of it in diphtheria has been still further carried out with some success, but peroxide of hydrogen appears to outrank it in this application. Dr. Lennox Wainwright justly extols its use in the nasal form of hay fever, when mixed with ammonium carbonate and used as a smelling salt. The distressing symptoms are many times permanently relieved. One of the most recent uses to which it has been put is in the treatment of laryngeal and pulmonary affections. Dr. Walker Downie explains its mode of action,—first, locally, as an anaesthetic which relieves the cough accompanying the affection; second, as a decided stimulant without harm to the parts; and last, as an antiseptic, for, being extremely volatile, it is readily diffused throughout the lung. By this use the antiseptic is brought as closely in contact with the affected parts as is possible. Certainly by his form of treatment the majority of his patients have had marked relief, and some have actually been restored to apparent health.

Methyl and **Methylene** are two terms which with their affixes are hopelessly confusing to the practitioner. Rival manufacturers, eager to obtain predominant recognition, so manipulate terms that it is almost hopeless to get reliable clinical reports from the action of these various, but more or less similar, agents. A little explanation of each may not be out of place here. "Methyl blue" is an anodyne and anaesthetic, considerably employed with some success in the treatment of diphtheria. "Methyl violet" is pyoktanin, the new antiseptic of last year, which will be spoken of later on in this commentary. "Methyl chloride" is strictly a local anaesthetic applicable to neuralgias, and not an anaesthetic for inhalation. "Methylene chloride" is the anaesthetic so long used by Sir Spencer Wells with such remarkable success, and which everybody else, pretty much, is afraid of. It is claimed to be a mixture of one volume of methyl alcohol and four of chloroform. "Methylene bichloride" was brought forward recently as a local anaesthetic liquid, differing from the last in not being a mixture, but a definite compound by itself. Lastly, "Methylene blue" is an anodyne and anaesthetic similar in action and in other respects to "Methyl blue," having been used in treating diphtheria with results like those obtained by the latter.

Microcidin (sodium naphtholate) is another of the newest antiseptic agents. It is a white powder obtained by the combination of B-naphthol with caustic soda, consisting in great part of naphtholate of soda, and for the remainder, of naphtholic and phenolic compounds. It is soluble in water, not caustic, and costs less than many of the other antiseptics. Dr. Berlioz states that it is somewhat inferior to corrosive sublimate and naphthol, ten times greater than carbolic acid, and twenty times greater than boric acid, in its antiseptic power. Ulcers and suppurating wounds rapidly cicatrize, and gangrenous surfaces are effectually deodorized after washing with a 0.3 per cent. solution. The French only give reports of its successful use since its introduction. Little is known of it as yet in England or in this country.

Orexin Hydrochlorate (phenyl-dihydro-quino-azoline), the agent introduced last year by Prof. Penzoldt, of Erlangen, to promote the appetite, has met with rather conflicting results in its administration, and at one time it was about to be discarded as of little use, when its introducer came to the rescue in an explanation of its failures as being due to its administration in gelatin-coated pills, as first recommended by himself. He claims now that the gelatin is in some way acted upon by the drug, and thus renders the whole insoluble in the stomach. He finally recommends it to be given in starch-paper wafers. Success appears to have followed from its use since, by several prominent observers; but surely it must be difficult to determine accurately the extent to which appetite is promoted in the economy by any one agent, when so many things have to be taken into account. Orexin hardly has a very promising future.

Paraldehyde has become well established with the medical profession, and serves as a serviceable alternate for the other hypnotics. It has recently been added to the British pharmacopœia. Reports from various quarters still differ as to its scope of usefulness. Its taste and odor are against it, and they always have to be masked in some way. There appears to be a difference of opinion as to a tolerance of the drug.

Peroxide of Hydrogen (H_2O_2) has increased very rapidly in usefulness during the past year, and, in fact, it has had a steady growth ever since its introduction. It is no doubt the most powerful of all antiseptics and disinfectants. There are now several good manufacturers of the article, which creates a healthy rivalry, and thus a reliable article is pretty sure to be kept on the market. It has been used to a considerable degree in diphtheria and throat and lung affections for the past year or two, and up to the present time has rarely failed to do its work. When it does fail, it will be found to be due, in the majority of cases, to lack of care in keeping, or attempting to use from the remainder of a bottle which has been long kept and possibly often dispensed from, and thus repeatedly exposed to outside air and the dust and dirt accompanying it. Surgeons in general, and obstetricians and gynæcologists in particular, are appreciating its usefulness more and more.

Phenacetin has justly grown in favor during the past year. It had a slight set-back at one time, due to a poisoning case, but it was finally found that it had been mixed with acetanilid for commercial gain, as the prices of the two vary considerably. It has now become official in the British Pharmacopœia. Great and increasing success has been met in the treatment of typhoid fever. In one report sixty cases were treated, and only one death occurred. In the fatal case, however, the patient did not get the drug until three weeks after the beginning of the attack. There were no serious complications in any of the cases where the drug had a full chance—that is, in the fifty-nine cases. Whooping cough has been aborted quite successfully. Its effects in the first stage of influenza are very marked. Its action is prompt and striking. It rapidly cures the headache in the majority of cases, aids in reducing the temperature, and somewhat relieves the sore and tired feeling of the limbs, but not completely. A large mass of testimony in its favor has now accumulated from the two recent epidemics of la grippe. It has been used in nearly every variety of pain with remarkably good results. Large doses have been employed repeatedly with favorable results in acute rheumatism, particularly that due to gonorrhœa. It apparently rarely fails, in its sphere of usefulness, no matter when used; it is cheaper than antipyrin, tasteless, and, from the extended experience of many, it is quite free from the unpleasant after-effects of antipyrin, such as depression of the heart and the rash which often follows. A very minor objection, however, in comparison with so many good points, is its comparative insolubility.

Phenocoll is the abbreviated name for phenol-glycocoll, and is one of the very newest antipyretics. It is a very interesting compound, for the reason that the German chemists have gone about the matter very systematically to construct this compound synthetically, with the aim of producing the very definite therapeutic effects sought for. Antipyrin is known to produce unpleasant after effects, phenacetin is too insoluble, and acetanilid combines both disadvantages. The problem, then, was to produce a compound that should unite the best properties of antipyrin and phenacetin. The simplest way of rendering phenacetin soluble, at the same time retaining its non-toxic and antipyretic properties, seemed to be to introduce an acid-forming radicle. This was done, and the result expected was accomplished. This base, phenocoll, is capable of forming salts, and the hydrochlorate is the one to be used in medicine, and is readily soluble in sixteen parts of water. This ready solubility at once gives it a decided advantage over most of the other antipyretics. Being such a new agent, of course it has little clinical history yet. It has been tried in Europe in cases of typhus fever, pneumonia, phthisis, and rheumatism, with most satisfactory results if foreign reports may be believed. Dr. Hertel, surgeon-major, who is one of the earlier clinical investigators with this agent, treated a small number of cases, to be sure, but he met with such good results that he urges the profession at large to give it a thorough trial. He lays great stress on the fact that the kidneys are not affected. In some cases where antipyrin, sodium salicylate, phenacetin, and acetanilid had been used with very little benefit, prompt relief was furnished with phenocoll hydrochlorate. When the article can be produced in large enough quantity to allow a very general use by the profession, great results are looked for.

Piperazin is the contracted name now given to the new uric acid solvent introduced last year under the name of piperazidin. When first introduced, it was supposed to be a synthetic spermin, but this is now doubted for several reasons. It is obtained in colorless and nearly tasteless crystals, and is easily soluble in water. It is not only much more soluble than lithium carbonate, but it will dissolve twelve times more uric acid. On theoretical grounds, then, alone, we can easily infer what result might be looked for after its administration. It has been tried experimentally by several continental observers, and found to come up to expectations sufficiently to deserve more extended trials. One French observer, however, claimed, from clinical observation, that uric acid was increased and urea diminished, but this was not afterwards verified. Its sphere of usefulness would appear to be in the treatment of gout and all kidney affections, although it has been tried with success as a diuretic and in a case of lead poisoning and a case of vesical ulcer. The dose used appears to have been about eight grains internally up to a daily maximum of about twenty-five grains. Subcutaneously five grains are used. The hydrochlorate apparently is the salt preferred, although the base is itself used. It gives no evidence of being toxic in its action. Reports are as yet very meagre from English and American observers.

Pyoktanin (methyl-violet) is the newly adopted trade name given to one of the anilin dyes long used for staining bacilli and micro-organisms ; it is now believed to have a destructive action on these organisms, and it has been put forth as a new antiseptic and bactericide. There is another form called the yellow. Each is used for special purposes. The former seems now to be preferred in surgical operations generally, and the latter in opthalmological in particular. Its pus-destroying property, from which it derives its name, is apparently well established at this time, but it has not shown uniformly good results otherwise. However, there are observers now who claim that it has little effect, if any, on suppuration, and the staining of the hands and clothes which accompany its use is strongly against it. This latter objection, however, has been met somewhat by the suggestion that these stains may be removed by soap-lather well rubbed in, and washing or brushing off with alcohol. It has been employed in the treatment of cystitis with some favorable results; but in general urethral injections, where much good may follow, Mr. F. F. Burghard, of King's College hospital, claims that too strong solutions are recommended. He advises beginning with a solution not stronger than 1 to 3,000, and gradually increasing up to 1 to 1,500, otherwise irritation and scalding on micturition occur. On open wounds and ulcers, the powder is simply dusted on with good effect, and where they have become septic this agent is more efficacious than any other antiseptic. Remarkable success is reported from abroad from its use on malignant growths; and even cancer has been experimented upon, both here and abroad, with the result of ameliorating the suffering and of acting as an effective deodorizer. In the various affections of the eye very diverse reports are on record, both in this country and abroad. In general, the majority acknowledge that some good effects follow its use, but it has not yet arrived at the surpassing value at which its introducer would figure it.

Quinine has recently been artificially reproduced by a species of transformation of cuprein, which is the alkaloid obtained from the bark of the remijia pedunculata, or cupra bark of central South America. It is mentioned here for no other purpose than that of general interest, for the discovery comes in one way some years too late, as at present the price of quinine is so comparatively reasonable that no incentive is offered to go out of one's way to produce the article other than from the cinchona barks. This production artificially, however, is another striking illustration of the marvelous results the synthetically inclined chemists of our day attain to. These chemists thought this construction out somewhat as follows: They knew cuprein formed definite crystalline salts ; they therefore produced the sodium salt. Then the possibility of substituting the sodium in this salt by a methyl group gave them reason to believe that the resulting compound would be quinine. This supposition proved to be correct, and resulted in a triumph for their endeavors.

Resorcin, one of the phenol derivatives, has stood the test of time remarkably well. Its most general use has been in skin affections, but good results have been obtained in whooping-cough and diphtheria, and in checking vomiting. Its anodyne effects may be increased until it acts in large doses as a hypnotic. Its antizymotic effects have proved very marked. There has been recently an increasing use in the treatment of the gastro-enteritis of children. It apparently arrests fermentation in the alimentary canal. It has an advantage over calomel when used in this affection by not increasing cardiac weakness. It has repeatedly given good results in cases of septic poisoning from post-mortem examinations. It has now been long enough on trial to become officinal.

Retinol (resinol) was discovered as far back as 1838, and is obtained by the distillation of Burgundy pitch or resin, and was known as resin oil. It has been used in surgery for some years back, in a limited way, as a good solvent for such agents as naphthol, camphor, or salol. It has recently been brought into more extended use, particularly on account of its being found to be a good solvent for quite a number of agents much used in surgery, It is not soluble in water. It is a good antiseptic, and is not irritating. It oxidizes very slowly, and its keeping properties are thus of high value. Phosphorus dissolved in it keeps remarkably well. It is now used very largely in skin affections, with good results. In gonorrhœa, particularly in the male, injections have proved of great service. Its use is increasing very fast.

Saccharin is the coal-tar derivative introduced some years ago, and interesting now from the fact that the English have added it to their pharmacopœia under the name glusidum (gluside). Its value appeared to be fully recognized, for three-quarters of the delegates from the British Isles to the Medical Council recommended the addition of this article. Its value as an antiseptic, which seems to be of some importance, was rather secondary to its remarkable sweetening power. Its relation to cane sugar is as 1 to 300.

It is a patented article, and this is one of the reasons why we do not hear more of it in this country, as the profession rather properly avoids patented articles ; but an important additional reason is found in its variability in strength owing to adulteration. Its use in the diet of diabetic patients, and of those in whom, for other reasons, sugar is limited, should lead us to use it to a larger extent than we feel disposed to at the present time.

Salipyrin (antipyrin salicylate) is not a new compound this year, but it is interesting from the fact that observations at the dispensing counter led to its discovery. Antipyrin and sodium salicylate liquefy when mixed together, and Prof. Spica, of Florence, found that from the resulting liquid antipyrin salicylate was obtained. From that time it has been sold under the coined name of salipyrin. It has been used as an antipyretic with better effect in intermittent than in continued fevers. Its general use in quite all of the various forms of rheumatism has met with some favorable results ; but, looking at the total for the year, they cannot be called remarkably encouraging. The price of the article has been somewhat against its general use, and many would claim that corresponding beneficial results may no doubt be reported from the administration of the antipyrin and the sodium salicylate separately, and in the varying proportions of each which the individual case might call for.

Salol (phenyl salicylate), the result of the combination of salicylic and carbolic acids, is not new, as it was prepared by Nencki in 1883, and introduced several years later. The hope previously expressed, that we had at last found a remedy of service in cholera, has hardly been fulfilled, as the reports now are quite at variance. Reports come from special cholera hospitals with very little encouragement, while, again, from individual private practice much good is obtained. It continues to be used in typhoid fever with favorable results. From South America reports come of its being a reliable agent in accomplishing intestinal antisepsis in the diarrhœa of children when complicated by malaria. In France, observers meet with success in treating diseases of the urinary passages with salol. Its great claim is, that it holds in composition its two ingredients until it reaches the locality in the economy where its usefulness is needed, and there splits up into its component parts and accomplishes its good results. The proportion of carbolic acid there present, however, has its dangers, which are too well marked by sad experience. It is no doubt an irritant to the kidneys, as repeated evidence is given in the reports of nephritis due to the carbolic acid set free. Poisoning symptoms are often seen, and now many fatal cases are recorded. The general conclusions to be drawn, then, would be, to use the agent with great caution, and avoid too prolonged use.

Somnal is the hypnotic introduced last year, and is said to be made by the union of chloral, alcohol and urethane, and resulting in a complex but definite compound with the above name. It is now questioned whether this is a definite compound as stated, since investigators now claim that they find it is simply a mixture. However this may be, the report of some observers are so partial to its use that it would appear that each component part has a beneficial and modifying effect on the other, thus giving results which are not obtained by the parts themselves. The pretty general opinion at this time is, that it is a safe hypnotic, less depressing, perhaps, than chloral, and serves as a good alternate to use for the other agents of its class.

Spermin, which received such marked attention from Dr. Brown-Sequard some time ago, and which was about dying a natural death, has been momentarily brought forward again by the recent announcement that the well-known firm of Schering, of Berlin, had succeeded in preparing it synthetically, and had registered this as a trade-mark word in Germany. They were supplying it to the profession in extremely small quantities, confining it largely to a limited number of hospitals and clinics for investigation and reports. Little has been reported as yet in regard to this artificial article, and what favorable reports have come to light may be explained away by other causes than this agent being present. Our verdict in this case would be very similar to that of Dr. Paul Werner, who says that the tonic effects were strictly psychical, the temporary increase in strength being due to the excitement of the experiments and to the confident hope of their good results. He further argues that similar results have been obtained by many forms of charlatanism.

Styracol is another new agent to be added to the now numerous ones to be used chiefly in the treatment of tuberculosis. It is described as the cinnamic ether of guaiacol. It is split up when taken internally, and the resulting component part, guaiacol, is supposed to be the effective agent. It is claimed to be a powerful antiseptic, promoting healing in open wounds and ulcers. Internally, good results are looked for in cases of chronic catarrh of the bladder, the stomach, and the intestines. It has no clinical history as yet to speak of, and the outlook is not very promising.

Sulphaldehyde is one of the newest hypnotics. It is a complete analogue in composition to paraldehyde, the oxygen of the latter being simply replaced by sulphur. It is an oily substance, with a disagreeable odor, obtained by the action of sulphuretted hydrogen on ethylic aldehyde in aqueous solution. As yet it has only been tried on animals,—frogs and rabbits,—and was found to produce a quiet, deep sleep, without any symptoms of excitement. It acted more powerfully than paraldehyde. It is completely excreted by the urine, to which it gives its characteristic odor.. We may hear from this agent during the coming year.

Sulphonal is one of the usually safe hypnotics which has had very wide use, and has largely increased during the past year. Two of its properties of great merit are its odorlessness and almost tastelessness. Its effect has been noticed to last over to a second and third night; and if this peculiarity is noted, it has its evident advantages as well as disadvantages. Italian observers have mentioned favorable results in diabetes. It diminishes the quantity of sugar, the polyuria, and the thirst. They also have noticed its good effects in either greatly diminishing, or entirely suppressing, the night-sweats in phthisis. Dr. D. D. Stewart, of Philadelphia, recommends it to be taken thoroughly dissolved in as hot an aqueous solution as agreeable. Sleep is then induced very soon after taking, and thus is avoided the usual delay of an hour or more before the effect is ordinarily produced. Dr. W. H. Gilbert, of Baden-Baden, reports danger from its popular and steady use. It is surely bad practice to leave the matter in the patient's hands to the extent of directing him to take a certain dose whenever he cannot sleep, as is apparently the practice with some. There are evidences now on record of the habit being established approaching that of the morphia habit. Fatal cases also have been reported during the past year. For such an effective and widely used hypnotic, then, the conclusion should be to use caution.

Thiol is the patented product obtained by heating the hydrocarbons in ordinary "gas oil" with sulphur until sulphuretted hydrogen ceases to come off, and then adding an equal weight of sulphuric acid. This was introduced last year as a substitute for ichthyol, and used principally in skin affections. It is now used in practice both in a powdered form and in a concentrated aqueous solution. Its odor and taste are not quite so marked as ichthyol, but its general physical character is similar. It also does not stain so badly as ichthyol. Gottschalk now gives the results of his nine months' experience with the agent in inflammation of the uterus and its appendages. He used a ten or twenty per cent. solution in glycerine. Large pelvic exudates have been made to disappear in a few weeks. Inflammatory erosions about the vagina are treated as successfully by applications of the powder. The uterine colic which often follows the application of iodine to the endometrium does not follow from the use of thiol solution.

Thymol, the product of the fractional distillation of the volatile oil of thyme, obtained from the plant thymus vulgaris, has long been used as a substitute for carbolic acid in its varied applications, with the great advantage of having a less disagreeable odor, and causing no pain, as it is not irritating.

It has recently found a new use in the treatment of chyluria dependent upon filariae in the blood. As a remedy for this affection has long been sought, the favorable report by Surgeon-Major E. Lawrie, of Hyderabad, of a cure of two cases is worth noting.* The important practical point noticed was that thymol destroyed the organisms present in the system. Reasoning *a priori*, Dr. Lawrie tried it extensively in diseases such as leprosy, phthisis and gonorrhœa, but without success. His conclusions, then, are, that either thymol acting evidently as a fatal poison to the filaria is not a poison to the bacillus, which seemed to him very unlikely, or the bacilli are not the cause of the diseases above mentioned. Other cases are now necessary to corroborate Dr. Lawrie's good results.

Tinctura Ferri Chloridi has not given for the past year or two the favorable results formerly derived from the preparation, and many practitioners have asked the cause. It may be found largely in the official preparation as laid down in the United States Pharmacopœia of 1880. The United States Pharmacopœia of 1870 very properly authorized an excess of acid to remain present in the freshly made product, and directed it to be set aside for a prolonged period. Thus, ethers were developed which were markedly beneficial, especially in cystitis and other bladder complaints. The present United States Pharmacopœia of 1880 directs only sufficient acid to be used in the preparation to make the reaction complete. Thus, a sample of this latter preparation which has stood aside from three to six months has no more ethereal odor than when freshly made. It is to be hoped that the present Revising Committee now at work will remedy this defect and return to the old formula.

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*The Lancet, vol. i., for 1891, page 864.

"**Tuberculin**" (Koch's liquid) is a brownish, syrupy liquid of about the color of a weak iodine solution. It is supplied for clinical purposes—principally to hospitals—in white glass, well-corked bottles, containing about fifty grammes. The solution for immediate use is then made up freshly, as needed, of one per cent. strength, with sterilized distilled water. The dose varies from a few milligrammes up to one gramme of the diluted solution. The injections are made with any hypodermic syringe, but preferably with one with Koch's modification.

As all well know by this time, considerable attention has been given to this agent by investigators and writers since its unexpected and, for the time, undesired presentation to the world. There is now little doubt that Prof. Koch would very much have preferred to keep the preliminary results of his investigations entirely within the circle of his own little band of co-workers until he should feel that the proper time had arrived for their promulgation; but a somewhat pardonable desire, on the part of the medical as well as the secular press, to spread the news of a possible cure for one of the most destructive enemies to humanity, set the whole world ablaze with enthusiasm over such a prospective triumph, and led us all into that inevitable error, which we almost invariably fall into every time a new remedy is introduced, of making very erroneous and extravagant deductions, and thus doing harm to the very subject we would desire to see advanced. We should all have no little sympathy for Prof. Koch in this predicament, which we have actually forced him into, and make due allowance for the presumptive manner in which the subject now so vital to his reputation was so prematurely handled. It has been recently given out that he proposes shortly to publish a third communication on his treatment, and to make known the long wished for manner in which "tuberculin" is prepared.

Prof. Koch has many enthusiasts in his behalf in the medical world, and, naturally, many skeptics; but all fair, conservative minds, not carried away for the moment by unlimited desire for novelty, and who have the advance of the true science of medicine at heart, cannot fail fully to agree with Prof. Rudolf Virchow, when, in debate before the Prussian House of Deputies in Berlin, last summer, on the granting of additional funds for Koch's Institute for Infectious Diseases, he said,—"I have never expressed any opinion to my professional brethren on the fundamental value of Koch's method, simply because I do not know how such an opinion can be formulated. I have only communicated a series of personal observations, which have indeed been of service in directing attention to one part of the question, and have especially enforced the need for calm and objective study that is so requisite in these difficult subjects. * * * The question has, in fact, been developed in unexpected directions, leading in many quarters to the hope that very striking results can be produced by those powerful measures — a hope which we cannot yet say has been annihilated. As a matter of fact, there is not a single case known in which any form of tuberculosis has been cured by this means. All cases which were for a while regarded as cured have afterwards been found to relapse; the improvements were merely temporary, such as often occur under other treatment. On the other hand, there is no doubt whatever that many serious dangers have been revealed, with regard to which I may claim some merit for myself. I have not yet seen any need to retract one word from that which I wrote at the end of January, in compliance with a ministerial request. * * * No doctor who feels called upon to make further trial of the remedy could by any possibility lay himself open to prosecution. The original trials were, in point of fact, made after results had been obtained in animals, which seemed to justify the expectations that were raised regarding the discovery." The year to come will no doubt show which way the tendency lies.

Urethan (ethyl carbamate) has grown greatly in favor during the past year, and justly so, for it proves itself more and more to be a mild hypnotic, with rarely a disagreeable sequence, and usually successful in all cases of insomnia not due to pain. In a few cases its effects have proved uncertain; but this occurs with most mild remedies. Under proper directions it is a very safe and effective hypnotic to give children.

Veratrum Viride has not received the attention it deserves, for the past few years. The reason is hard to find, unless it be that the profession has been so much occupied with the consideration of the overwhelming number of novelties that this well established and long tried remedy has fallen into comparative disuse. Its quality, and that of its preparations, have not deteriorated in the least, and therefore the profession should make use more largely of its beneficial action. It has always proved of marked value in the treatment of pneumonia; and, to bring up the subject again before the profession, we find Dr. T. G. Stevens, of Iowa, has made a study of the drug, and has published his results. His notes deserve perusal, if for no other reason than to kindle a renewed interest in its use.*

Weights and **Measures** are subjects which have received considerable attention from scientific men generally in this country for the past few years. They are now of renewed interest, as very decided steps have recently been taken to further the change from our confusing and cumbersome American system to the more rational, and in the end easier, decimal, metric, or French system, as it is variously called. The latter is as much superior to the former for ready comprehension and easy translating from one grade to another as our present monetary system is to the English. The English themselves are now beginning to see the disadvantages of their old system in the line of trade with other nations, as, with the exception of our own country, most other nations use the metric system.

Our government, two or three years ago, very properly saw fit to legalize the metric system, and it is now, in fact, the only system authorized. It is in use in the navy department, the marine hospital service, the coast survey, and the post-office.

In September, 1889, the American Association for the Advancement of Science appointed a committee to promote and urge the use of the new system among all scientific bodies and individuals. They have been diligently at work, and now fruits of their efforts are evident in every quarter.

One of the most important recent advances to the pharmaceutical and medical professions occurred in the Convention for the Seventh Decennial Revision of the United States Pharmacopoeia, held in May, 1890, when, by an almost unanimous vote, it very definitely directed the Revision Committee to adopt the metric system exclusively.

It therefore now behooves us all to see to it that we make ourselves thoroughly familiar with the working of this new system, and all who have used it at all practically will surely predict a universally preferred system.

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*Gaillard's Med. Jour., vol. lii., page 210.

ON THE APPROXIMATE ESTIMATION OF UREA IN URINE.*

In January, 1884, the writer published a paper under the above caption (see Ephemeris, page 438). In this paper, after briefly reviewing the character and importance of the subject,—its difficulties, and what had already been done,—a simple apparatus and method were offered whereby the process was brought within reach of the physician and well trained nurse, to be applied in the physician's office or in the sick-room. The advantages claimed for this method were first, its simplicity of construction from materials within easy reach of all;—second, that instead of attempting to measure the evolved nitrogen gas,—a proceeding requiring special apparatus, and almost beyond the reach of the ordinary physician,—the volume of water displaced by the gas was measured;—third, that instead of handling substances so inconvenient, troublesome and dangerous to inexpert persons as bromine and caustic soda, a reagent for decomposing the urea was substituted that was much more simple and convenient, free from trouble and danger, and to be found ready prepared almost anywhere. This reagent was the common Solution of Chlorinated Soda of the U. S. Pharmacopœia from the revision of 1840 to that of 1870 inclusive.

From the need of such a device for common clinical use this apparatus soon went into occasional use, not only in this but also in other countries, where the importance of its use was recognized, and during the past eight years favorable reports of its use have not been very infrequent.

But now, on reaching home after an absence of twenty months, the writer very unexpectedly finds a paper on "Quantitative Tests for Urea by Dr. J. C. Bierwirth," published in "The New York Medical Journal" for November 21st, 1891, page 568. In this paper Dr. Bierwirth shows conclusively that in his hands, and in other hands, the method is very inaccurate and very variable in its inaccuracy, and commonly does not give account of the urea present by from .75 to 1.00 p.c., and from his experience he believes that Solution of Chlorinated Soda as a reagent for the decomposition of urea is not trustworthy.

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* Read before The Kings County Medical Association at the meeting of March 8th, 1892, by E. R. Squibb, M. D.

Upon referring to his notes and his published paper, this writer felt very sure of his facts and results upon which the statements of his paper were based, for they had been abundantly verified by subsequent experience, but he had full confidence in this part of Dr. Bierwirth's work, and knew not how to account for the discrepancy, especially as Dr. Bierwirth had used Solution of Chlorinated Soda that was known to be fully up to the U. S. P. standard. Investigation was at once begun and the cause of the difficulty was soon found at a point least suspected. In the revision of the U S. Pharmacopœia for 1880, published in 1882, the proportions of the ingredients directed for making the Solution of Chlorinated Soda had been changed, and no notice of the change had been given because the strength in available Chlorine was not changed, and available Chlorine was supposed to be the only standard of value in the preparation.

The Solution was admitted to the U. S. P. in 1840, and from that time until 1880 the proportions were 24 parts of Carbonate of Sodium to 12 parts of Chlorinated Lime, but in 1880 they were changed to 25 parts of Carbonate of Sodium to 20 parts of Chlorinated Lime,—a reduction of 60 parts of the sodium salt in 160. In former revisions the sodium salt had been in large excess of what theory required, and this excess was judged to be useless and was left out, while the available chlorine remained as before. As the Committee of Revision knew of no other use for the Solution than that of a disinfectant, and knew of no disinfectant effects from the excess of Carbonate of Sodium, they knew of no change by leaving out this excess, and therefore gave no notice of change. In this change they followed the German Pharmacopœia, adopting its proportions. In the judgment of the writer this change was a mistake. The preparation is a loose combination of its elements, and undergoes internal molecular change by keeping, but the analogy of many other better known instances in which an excess of one element prevents or retards change, leads to the probability that the excess here is important. And, it is not improbable that the excess plays an important part in the disinfectant action.

It is however now very certain that while the Solution of 1870 and revisions previous to that, having the excess, will decompose urea completely, the Solution of 1880, not having the excess, decomposes urea only partially, and this where both Solutions have the same proportion of available chlorine, and the one answers perfectly for the writer's urea apparatus, while the other does not.

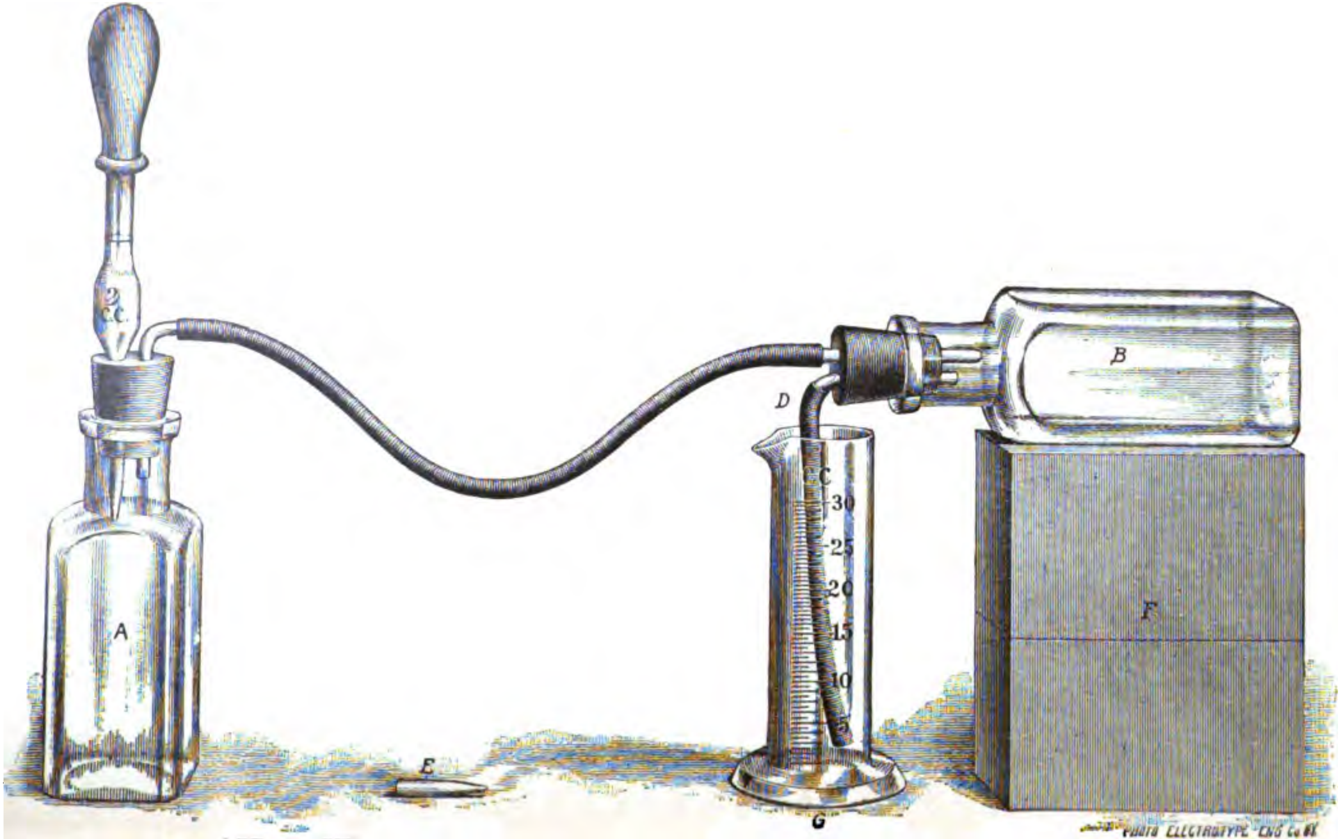
And this difference in the Solution, is the sole reason of the difference in the results obtained by Dr. Bierwirth and the writer, and the failure of the method is due, not to the apparatus, but to the reagent used in it. The original work of the writer was done late in 1883, and although the U. S. P. of 1880 was published in 1882, the change in making this Solution was not made until 1884, and was then made—not through any appreciation or knowledge of the character of the change, but simply in obedience to the general practice of following the Pharmacopœia as a standard. How blindly this was done is still farther shown by the fact that this very formula and process of 1880 was reviewed by the writer in 1885 (see Ephemeris, page 809) without noticing the change that had been made, the review having been directed to the Solution only as a disinfectant.

The change, then, being unknown and unsuspected, and its relation to the decomposition of urea, being, of course, also unsuspected, the writer made in his original paper the blundering and inaccurate statement that solutions made by either the Pharmacopœia of 1870 or of 1880 would answer very well for the urea estimation, when had the solution of the later revision been critically tried, as has now been done by Dr. Bierwirth, it would have failed of course. How far those who have used the method may have been misled by getting the wrong reagent it is impossible to say, but it is a fortunate accident that the error being one of understatement was on the safe side.

The writer is very much indebted to Dr. Bierwirth and thanks him heartily for having exposed this error, as, had he not taken the subject up it might have gone on indefinitely.

As the subject of the estimation of urea is one of increasing importance to the physician, and as this writer has now had some years of additional experience and reading upon it, it is considered worth while to go over the subject afresh and offer some improvements that have been made in the apparatus and method which may adapt it better to a more general use, and at the same time give some choice of reagents in order that they may be checked against each other when this is desired.

First of all, it cannot be too strongly insisted upon that these rapid methods which are based on the decomposition of the urea and the measurement of its evolved nitrogen as the indication of its quantity, afford approximate results only. There are several errors incident to such processes in ordinary hands which are prac-



APPARATUS FOR THE APPROXIMATE ESTIMATION OF UREA IN URINE.

tically inevitable, and their due consideration shows conclusively that the general range of error can hardly be less than 0.1 p.c. above or below the truth, and should not be greater than about 0.2 p.c., plus or minus. That is, when a solution of pure urea of known strength is tested, the range of admissible error will not generally be less than 0.2 p.c., nor greater than 0.4 p.c. when 1 cubic centimetre is taken for assay, and about half that range when 2 cubic centimetres are taken.

APPARATUS.

The improved apparatus now offered is in principle and general design, the same as the old, but the quantity taken for the estimation is 2 Cc. instead of 4, and therefore the vials are reduced to half the size formerly used. This is done, without materially increasing the error, by having a much smaller and more accurate capacity pipette, and by making this take the place of the urine jar by passing through the stopper, as shown in the cut. Then a graduated jar receives the water displaced by the gas, and measures it directly with more accuracy and convenience than the graduated pipette.

The pasteboard box which contains the apparatus shown in the cut also contains a bottle of good chlorinated lime sufficient in quantity for forty testings. This bottle is dated on the bottom, so that the age of the contents may be known. The lid of the box serves as a support for the bottle B. The box also contains a card with directions for the use of the apparatus. Another card with directions for making the different reagents, and a third card with urea table for interpreting results.

A large measure for taking the measure of daily urine, and two ordinary half-pint bottles for mixing the reagent, are needed but not included with the apparatus.

In using the apparatus put the reagent for decomposing the urea into bottle A. Then measure exactly 2 Cc. of the urine in the pipette. To do this properly first dip the mouth of the rubber bulb into water, to lubricate it, and then slip it onto the upper end of the pipette nearly as far as it will go. Compress the bulb upon the pipette and dip the lower end of the pipette into the urine. Then relaxing the compression entirely the bulb will expand and the urine will rise in the pipette to fill or nearly fill the body of it. Then, holding the body firmly between the left thumb and finger, take the rubber ring at the mouth of the bulb with the right thumb and finger and screw the bulb upward on the pipette until the urine rises to the mark,—the lower limb of the meniscus to lie exactly upon the mark—the lower point of the pipette being still kept immersed in the urine. Then raise the point out of the urine, and screw the bulb a little higher on the pipette until a little air is drawn in at the point below. This avoids the risk of loss of urine from the point in case any expansion of the air in .the bulb should force the urine out at the point. It is essential to the best management of this step not to attempt the adjustment to the mark on the pipette by compression of the rubber bulb, nor by sliding the bulb directly up and down on the tube, but by screwing it around, touching only the solid rubber ring at the mouth of the bulb. To recognize the importance of all this detail for accuracy in measuring, it is only necessary to mention that some degree of error is inevitable under even the best practicable management, and that this error is multiplied from 500 to 600 times in applying the results of the assay to the total urine of 24 hours. And in processes where only 1 Cc. of urine is taken for assay the same error is multiplied from 1000 to 1200 times. The pipette when thus carefully charged, is pushed through the vacant hole in the rubber stopper for bottle A, which stopper has just been dipped in water. This pushing through the wet stopper wipes off the urine from the outside of the pipette. The stopper thus prepared, is then put into its place in bottle A. One end of the long piece of rubber tubing C, is then dipped in water and slipped onto the bent glass tube of bottle A and from this it need not again be removed in subsequent testings. Next, fill bottle B full of water of the temperature of the room, and then having slipped one end of the short piece of rubber tubing D onto the bent glass tube of the rubber stopper of B, push the stopper into its place in the bottle, allowing the displaced water to escape through the tubes. Then holding bottle B in the right hand with the forefinger over the end of the straight glass tube, incline the bottle toward the bent glass tube until that and the rubber tube upon it fill with water. When filled stop the flow of water from the rubber tube D by closing the straight glass tube with the forefinger, and with the left hand put the little glass stopper E into the free end of the rubber tube D while this tube is full of water. Then lay bottle B, thus charged, on its side, upon a support F, as shown in the cut, and slip the free end of the long rubber tube C, from bottle A, onto the end of the straight glass tube of the stopper of bottle B, thus connecting A and B. Next remove the little stopper E from the end of the short rubber tube D, when a few drops of water will escape, and a few bubbles of air will enter B from A. But, if the apparatus be tight and be at the room temperature, no more water will run out nor will any air enter. Next, the measuring jar G is put under the short rubber tube, and this tube is lengthened or shortened by slipping it down or up upon the glass tube, until the end just clears the bottom of the graduated measuring jar; and now the apparatus is ready for the process.

THE PROCESS.

Taking bottle A in the right hand compress the rubber bulb between the left thumb and fingers until the entire contents of the pipette are forced into bottle A with the reagent, and see that the last drop be forced in. Then still holding the bulb compressed, shake the lower part of the bottle A from side to side, and not up and down, for, beyond an accidental drop or two no liquid should get into the long rubber tube C, to be carried over by the current of gas into bottle B. The reaction begins promptly, and while the gas is actively passing over into bottle B, the compression of the rubber bulb of the pipette is to be gradually relaxed, and the thumb and finger which compressed it are lowered to hold the lip of the bottle A. This part of the bottle is now kept fairly steady, while the lower part is pretty actively shaken from side to side, and this shaking is to be continued as long as any bubbles of gas come over into bottle B. But if the shaking has to be continued longer than about ten minutes, the warmth of the hands will so warm the bottle A as to expand the air inside, and cause a slow passing over of small bubbles. In cases of slow or indefinite end reaction, where ten or twenty minutes of shaking is required to make sure of the result, it is much better to have recourse to a warm bath for the bottle A. A bowl of hand-warm water, not above 40°C.=104°F., or thereabout, is to be used, and the bottle A being immersed in this, is occasionally taken out and shaken, until warmed up to the point where no more gas passes over. This will shorten to six or eight minutes a process which would otherwise go on, by slow end reaction, for half an hour. Whether the warm bath be used or not, the next step of the process, after bubbles have practically ceased to go over, is to immerse bottle

A in a bath of water at the room temperature for four minutes. A vessel of water sitting upon a table in an ordinary room, will, in five or six hours take and maintain a temperature of from 1° to 2°C. below the room temperature, and such a bath in which bottle A may be entirely immersed, must be provided for this step. When bottle A is so immersed, water from B will pass freely through tube C into A and be replaced in B by water drawn back from the measuring jar through tube D, and when these temperatures and pressures are practically balanced so that there is no longer any perceptible change of level in the measuring jar, the process is finished. This step requires about 4 minutes' immersion. The bottles and tubes are now lifted out and set aside, and the quantity of water in the measuring jar is carefully read off to one-half cubic centimetre.

EXPLANATION OF TABLE OF APPROXIMATE RESULTS.

Each Cc. of the water in the measuring jar represents a Cc. of the nitrogen gas evolved by the decomposition of the urea in the urine, and each Cc. of the gas represents 0.0027 gramme of urea when the Cc. of gas is measured at 0°C. and 760 Mm. barometric pressure. The pressure may be disregarded in this process, but the expansion by temperature may not, although it was disregarded in the former paper and table. By the law of Dalton and Gay-Lussac gases expand $\frac{1}{273}$ of their volume at 0°C. for every 1°C., and as the measurement for this process may be assumed to be at about 18°C.=64.4°F., that temperature is adopted here. Thus $\frac{1}{273}$ of its volume for each degree multiplied by 18°C. is equal to 0.065934, and therefore 1 Cc. of the gas measured at 0°C. measures at 18°C. 1.065934 Cc., and this it is that is equal to 0.0027 gramme (0.002688 gramme more exactly) of urea. Therefore from each Cc. of water as read off from the measuring jar, 0.065934 Cc. must be subtracted as a correction for temperature expansion. That is, the reading off is too high by this fraction from each Cc., and, for example, 15 Cc. as read off must be corrected by (0.0659×15=) 0.9885 Cc., or practically 0.99 Cc., and the true measure becomes (15—0.99=) 14.01 Cc., or practically 14 Cc. This correction is applied throughout in constructing the following Urea Table, and thus a nearer approach to accuracy is attained, while the troublesome calculations are avoided.

Again, as each Cc. of water displaced is equal to a Cc. of nitrogen gas which displaced it, and this, when corrected for temperature represents 0.0027 gramme of urea, the number of Cc. of water represents the number of times 0.0027 gramme of urea is contained in the 2 Cc. of urine taken for the assay. But to obtain a percentage of urea it is a little easier to take the results from 1 Cc. of urine and therefore the number of Cc. of displaced water is divided by 2. Then the number so obtained multiplied by 0.0027 gives the percentage of urea in the urine. For example, suppose the displaced water from 2 Cc. of urine taken be, after correction for temperature, 14 Cc. This divided by 2 gives 7 Cc. for each 1 Cc. of urine. Then 7 times 0.0027 is 0.0189 gramme. Then as this quantity of urea comes from 1 Cc. of urine, which is assumed to be 1 gramme, although it is a little more—the quantity must be multiplied by 100 to give percentage, and this is the same thing as moving the decimal point two places to the right, and thus 0.0189 gramme of urea becomes 1.89 p.c.—and in this way the percentage column of the following Table is obtained.

The first column of the Table gives the reading from the measuring jar after having been corrected for 18°C.=64.4°F. above 0°C.=32°F. And the second column gives the percentage calculated upon the reading after being corrected for expansion by temperature, and all the other columns are calculated from the corrected readings.

The third column gives the quantity of urea in grammes contained in each measure of 30 Cc. of the total urine of 24 hours' excretion; and the fourth column gives the quantity of urea in grains contained in each fluidounce of the total urine of 24 hours' excretion—both being only approximate because not corrected for temperature in measuring, and only for a fixed and arbitrarily assumed difference in specific gravity between water and urine. The measuring jar of this apparatus is graduated, with a fair degree of accuracy, to half cubic centimetres up to 30 Cc., and from this measure of 30 Cc., a fluidounce of water or urine can be pretty accurately poured out. The fluidounce of the common apothecary's measure is 29.52 Cc., but when a measure of 30 Cc. is poured from a measuring jar, enough liquid will remain upon the inside of the measure to reduce the quantity poured out to somewhere about the difference between 30 Cc. and 29.52, and therefore this difference is disregarded and 30 Cc. is assumed as a fluidounce (f ℥.). Then as the specific gravity of urine is always greater than water, a f ℥. of urine will weigh more than a f ℥. of water. But the s.g. of urine is very variable, and therefore for use in the Table a fixed s.g. must be assumed and that which is adopted here is 1.025 as compared with water as 1.000. This gives the weight of 30 Cc. of urine as 30.75 grammes and the weight of 1 f ℥. of urine as 467.4 grains, and these data are the bases for the calculations of the third and fourth columns.

The fifth column gives in grammes the quantity of urea in 473 Cc. = 1 pint of urine corresponding to each percentage result; and the sixth column gives in grains the quantity of urea in 1 pint of 16 f ℥. of urine, corresponding to each percentage result.

. The seventh and eighth columns may not be useless for casual inspection. It has been estimated that the average normal excretion of urine in adults for each 24 hours is not far from 1181 Cc., which is equal to 2.5 pints or 40 fluidounces, and the variation from this, above or below, is chiefly water. If, therefore, the excretion for 24 hours should be evaporated down to this quantity if above it, or be made up to it with water if below, and be then assayed for the proportion of urea, the results would be all that could be desired. Taking then 1181 Cc. or 40 f ℥., as an assumed standard, the seventh column gives in grammes, and the eighth column gives in grains, the quantity of urea corresponding to each percentage that would be excreted in 24 hours. The estimated average normal amount may be 30 grammes, equal to 462.96 grains, but "A range of from 20 to 40 grammes (308.6 to 617.2 grains) must at least be admitted in adults." (Tyson, edition of 1891.) It will therefore be seen that while the average normal excretion may be about 20 p.c. = 30.5 grammes = 471.2 grains, the range is a very wide one extending from 13 p.c. to 27 p.c. according to Tyson. This leaves only about one-third of the Table below the lower limit of normal health, and the ninth column gives a probable indication of the limits consistent with ordinary health in adults.

It is hardly necessary to say that the Table is one of approximative equivalents, and is read in horizonal lines.

One point should be always borne in mind in direct relation to any urea table, and that is, that all good authorities insist upon its being little more than a waste of time and labor to assay the urine of any particular hour of the day or night, and that unless a specimen of the total excretion of 24 hours can be had, the results are misleading and may be dangerously misleading. And farther, that for the best results, and those which are most trustworthy, the assays of several successive days should be taken.

TABLE OF APPROXIMATE PROPORTIONS OF UREA IN URINE, FOR CLINICAL USE.

One cubic centimetre of nitrogen gas at 0° C.=32° F. equal to 0.0027 gramme of urea.

Assumed room temperature for measurements 18° C.=64.4° F.

Rate of expansion 0.003663 times the volume for each 1°C. Correction applied for 18°C.=32.4°F. is (0.003663×18=) 0.0659 subtracted for each 1 Cc. as read off from the measuring jar, and the percentage is calculated from the corrected reading.

Thirty cubic centimetres is assumed as equal to one fluidounce, but in converting any considerable quantities from one measure to the other 29.52 Cc. should be taken as 1 f ℥.

In converting measures to weights, and in using measures and weights together, an assumed specific gravity for abnormal urine is taken; namely, 1.025 at 25°C.=77°F. and 30 Cc. of urine of such s.g. weighs 30.75 grammes, and 1 f ℥. weighs 467.4 grains.

Four hundred and seventy-three cubic centimetres is assumed as equal to one pint of sixteen fluidounces, and when these measures are used for urine they are assumed as weighing (1.025×473=) 484.83 grammes,—and (467.4×16=) 7478.4 grains, respectively.

The seventh and eighth columns must not be taken as having any definite relation to, or bearing upon the assay, excepting when the total 24 hours' excretion amounts to just 1181 Cc. or 40 f ℥. or very near to this measure, as the calculations are based upon this arbitrary quantity.

Reading of the measuring jar in Cc. (Corrected.)	Percentage of Urea.	Urea contained in 30 Cc. or 1 f ℥. of Urine.		Urea contained in 473 Cc. or 1 pint of Urine.		Urea contained in 1181 Cc. or 40 f ℥. of Urine.		Limits consistent with ordinary health in Adults (Probable.)
		In Grammes	In Grains.	In Grammes	In Grains.	In Grammes	In Grains.	
4 Cc.	0.50	0.1588	2.34	2.425	37.44	6.055	93.60	
5	0.63	0.1937	2.94	3.054	47.04	7.625	117.60	
6	0.76	0.2337	3.55	3.685	56.80	9.200	142.00	
7	0.88	0.2706	4.11	4.267	65.76	10.658	164.40	
8	1.01	0.3106	4.72	4.897	75.52	12.227	188.80	
9	1.13	0.3475	5.28	5.479	84.48	13.680	211.20	
10	1.26	0.3875	5.89	6.110	94.24	15.255	235.60	
11	1.39	0.4274	6.50	6.739	104.00	16.825	260.00	
12	1.51	0.4643	7.06	7.321	112.96	18.278	282.40	
13	1.64	0.5043	7.67	7.951	122,72	19.853	306.80	Lowest.
14	1.77	0.5443	8.27	8.582	132.32	21.427	330.80	
15	1.89	0.5812	8.88	9.164	141.28	22,880	353.20	
16	2.02	0.6212	9.44	9.794	151.04	24.455	377.60	
17	2.14	0.6581	10.00	10.376	160.00	25.907	400.00	
18	2.27	0.6980	10.61	11.005	169.76	27.478	424.40	
19	2.40	0.7380	11.22	11.636	179.52	29.053	448.80	
20	2.52	0.7749	11.78	12.218	188.48	30.505	471.20	Normal.
21	2.65	0.8149	12.39	12.849	198.24	32.080	495.60	
22	2.77	0.8518	12.95	13.430	207.20	33.533	518.00	
23	2.90	0.8918	13.55	14.061	216.80	35.107	542.00	
24	3.03	0.9317	14.16	14.690	226.56	36.678	566.40	
25	3.15	0.9686	14.72	15.272	235.52	38.131	588.80	
26	3.28	1.0086	15.33	15.903	245.28	39.706	613.20	
27	3.40	1.0455	15.89	16.484	254.24	41.158	635.60	Highest.

REAGENTS.

The reagents for the estimation of urea by measuring the nitrogen which results from its decomposition, are, thus far, only two in number,—the hypochlorites and the hypobromites. These are chemicals whose nature is not very well understood and they are characterized by the condition that their elements are so loosely combined as to be, under all ordinary circumstances, in a state of continuous molecular change. That is, they are unstable combinations of their elements, and upon this quality their utility in this process seems to depend. But they are not equally unstable. The hypochlorites are more stable, or change more slowly than the hypobromites, and therefore in this reaction for decomposing urea it is not necessary that they should be freshly made for each assay, or group of assays. But this characteristic which gives them this advantage involves the disadvantage that those of them which keep best are slowest in reaction with the urea, and give the longest and least definite end reaction. Both reagents with proper management decompose all the urea with evolution of all its nitrogen, and the quantity of urea decomposed is determined by the quantity of nitrogen evolved. Therefore, the object is so to manage the reagents as to decompose all the urea present, and to measure the nitrogen gas set free ; and now the different management for the different ways in which the reagents are used, is to be considered.

USE OF THE HYPOCHLORITES.

One of the chief advantages that induced the writer to offer this apparatus and process in his original paper of 1884, was the facility given for its use by the easy access, almost everywhere, to the Solution of Chlorinated Soda of the U. S. Pharmacopœia of 1870. This Solution is essentially a solution of sodium hypochlorite and of sodium carbonate, bicarbonate and chloride, containing not less than 2 p. c. of available chlorine, and the change which it undergoes by keeping seems to be the slow conversion of the sodium hypochlorite into sodium chloride, wherein the chlorine is no longer available, and into free oxygen. This change is, however, so slow that bottles of it put up over 25 years ago with 2 p.c. of available chlorine, are in the writer's possession containing 0.6 p.c. of available chlorine, while freshly imported Labarraque's Solution contains only 0.4 p.c.

The U. S. P. of 1880, however, changed the proportions of the ingredients, so that its Solution of Chlorinated Soda is essentially a solution of sodium hypochlorite and chloride with very little or no sodium carbonate or bicarbonate, and containing not less than 2 p.c. of available chlorine—that is, of hypochlorite not yet changed into chloride. There has not yet been time for long trial of the keeping properties of this Solution of 1880, but the writer believes that it changes more rapidly than the Solution of 1870. And, that the solutions are very unlike is proved by the very singular fact that although they have the same proportion of sodium hypochlorite, the one will completely decompose urea while the other will not. Then as the failure of the 1880 Solution was apparently due to the absence of the excess of carbonate and bicarbonate of sodium present in the Solution of 1870, as the only known difference in the formulas,—carbonate of sodium was added to the Solution of 1880, but with no influence upon its reaction with urea. But when proportions varying from 2 to 5 p.c. of sodium bicarbonate were added to the Solution of 1880, it decomposed the urea perfectly, but gave traces of carbon dioxide or carbonic acid in the evolved nitrogen, thus preventing its use in this way to render the 1880 Solution available, although the readings of gas obtained were only slightly too high. Another very singular observation, carefully repeated, was that sodium bicarbonate added in the same proportions to the 1870 Solution caused it to decompose the urea only partially, and to give traces of carbonic acid in the resulting gas. All this goes to show that the composition of these two solutions is not well understood in their relations to the decomposition of urea, and if here, the one is effective and the other is not, is it not probable that as disinfectants, in decomposing the hurtful matters in the secretions and excretions to which they are applied, the one may be more effective than the other? In short, the writer is inclined to believe that the reaction with urea may be regarded as a test of the disinfectant reaction upon other excrementitious matters, and therefore that the 1870 Solution is a better disinfectant, and that it keeps better, and he hopes the present Committee of Revision will return to the formula and process also, of 1870 for the Pharmacopœia of 1890. Whether the Committee does or does not return to it, the writer will return to it in his own practice, and will send out no other than the 1870 solution. But as this Solution will not be generally accessible while the 1880 Solution will be, and as the 1880 Solution will probably be continued in 1890, it is worth while to offer a formula and process for the extemporary preparation of the 1870 Solution by which any physician, pharmacist or nurse can, in about 3 hours, make about 330 Cc. or 11 f℥. of the solution that will keep in good condition for a year.

EXTEMPORANEOUS SOLUTION OF CHLORINATED SODA.

Take of good Chlorinated Lime ("Chloride of Lime") 24 grammes.
Sodium Carbonate ("common Washing Soda") 48 "
Water, a sufficient quantity.

Shake the lime salt very thoroughly with 200 Cc. of water and pour the thinner portion of the mixture upon a wetted paper filter, receiving the filtrate in a 500 Cc. bottle. Shake the residue of the lime salt with 75 Cc. more of water, and when the first portion is nearly drained through the filter pour on the whole of the second portion. When this has drained through, the clear filtrate should measure about 265 Cc., and if the filter be a good one the time required will be about 2 hours. Dissolve the Sodium Carbonate in 90 Cc. of hot water by agitation, pour the Solution into the bottle with the filtrate, shake well and filter. The filtrate should measure about 330 to 335 Cc.

This extemporaneous solution of chlorinated soda is substantially that of the U. S. P. of 1870, and answers very well for this urea process, and when made from ordinarily good chlorinated lime or "Bleaching Powder," 10 Cc. of the solution is quite sufficient for the reaction, and is better than a larger quantity. But if the lime salt be old and poor, or the Solution be old, 15 Cc. is a better quantity with which to charge bottle A, and with this reagent a warm bath will shorten the process.

SOLUTIONS OF PURE UREA.

For trials with the various forms of these reagents in this apparatus and process, pure urea, well crystallized, was taken, and its freedom from moisture was proved by keeping it over sulphuric acid for 48 hours without appreciable loss. From this 2.5 p.c. and 2 p.c. solutions were freshly made every few days during the entire two months over which the trials extended, and when any considerable growths occurred in the solutions they were not relied on.

CHLORINATED LIME, CHLORIDE OF LIME, OR BLEACHING POWDER.

In "The Pharmaceutical Journal and Transactions," London, for March 29th, 1890, Third Series, Vol. 20, page 793, Mr. D. B. Dott, F. I. C., F. R. S. E., has a short paper, in which he recommends Solution of Chlorinated Lime for the assay of urea. He takes one part of Chlorinated Lime and three parts of water, and filters off the solution from the insoluble part. With this solution he fills a nitrometer, such as is figured in the Ephemeris at page 1196, letting in the urine from the funnel, and getting very accurate results. A nitrometer is out of the reach of the ordinary physician and nurse, and not available for clinical use. But chlorinated lime is so largely used as a disinfectant that it is easily accessible of fair quality everywhere, and can be had without difficulty of the best quality and put up in glass, for best keeping, so that it is available and convenient for this apparatus if the quality can be depended upon. To test this point specimens in possession of the writer were tried for available chlorine,—that is, chlorine in the condition of hypochlorite. These were all put up in amber glass and the bottles wrapped in paper.

No. 1 was put up about December 27, and then contained 38 p.c. available chlorine. Now (March 1) it contains 38 p.c. There was therefore no appreciable loss in about two months' keeping.

No. 2 was put up May 4, 1891, and then contained 38 p.c. available chlorine. March 1, it assayed 29.9 p.c., and therefore lost about 8 p.c. of its available chlorine in ten months, and this is regarded as an average loss. Another parcel 16 months put up lost (34.7—25.2=) 9.5 p.c. of available chlorine.

Then 8 parcels were obtained from as many different sources, pains being taken to get some of them from pharmacies of small business, where they would be likely to be oldest. All excepting No. 10 were put up in either metal or pasteboard cylinders, well closed, containing one pound or half pound each, and the cost, retail, was 15 to 20 cents per pound. All were put up by two dealers, but one of them sold two brands. The first 4 were put up by one party and the remainder by the other. One other brand, only, is known in this market, but it was not met with in buying the samples.

No.	3	contains	26.3	p.c.	of available	chlorine.	Put up in	metal	cylinder.
"	4	"	26.2	"	"	"	"	"	"
"	5	"	18.2	"	"	"	"	"	"
"	6	"	35.4	"	"	"	"	pasteboard	"
"	7	"	26.3	"	"	"	"	metal	"
"	8	"	30.2	"	"	"	"	pasteboard	"
"	9	"	36.4	"	"	"	"	"	"
"	10	"	30.4	"	"	"	"	paper parcel.	

Two grammes from each of the first 5 samples were successively put into bottle A, well shaken in the bottle with 10 Cc. of water, and then used for the process with the 2 p.c. urea solution, but the results were only 1.72, 1.64, 1.51, 1.39 and 1.30 p.c., showing conclusively that the mixture without filtration would not answer for the process, although there is no known reason why it should not when the filtered solution answers well. Then from each of these ten samples 20 grammes was weighed off and well shaken with 60 Cc. of water in a measuring jar, and the mixture poured upon a paper filter in a funnel in a bottle marked at 100 Cc. When drained the residue was washed on the filter until the filtrate measured 100 Cc., and these solutions of chlorinated lime were kept for the process, each 10 Cc. representing about 2 grammes of each of the samples. Two assays were made with each solution, the first with 10 Cc. representing 2 grammes of the sample, and the second with 15 Cc. representing 3 grammes of the chlorinated lime of each sample.

The results were as follows, a 2 p.c. solution of pure urea being used.

No.													
1.	2	grams.	in	10	Cc.,	sample	cont'ing	33	p.c. available	chlorine,	gave	2.02	p.c
1.	3	"	"	15	"	"	"	33	"	"	"	2.02	"
2.	2	"	"	10	"	"	"	30	"	"	"	2.14	"
2	3	"	"	15	"	"	"	30	"	"	"	2.08	"
3.	2	"	"	10	"	"	"	26.3	"	"	"	2.02	"
3.	3	"	"	15	"	"	"	26.3	"	"	"	2.08	"
4.	2	"	"	10	"	"	"	26.2	"	"	"	2.14	"
4.	3	"	"	15	"	"	"	26.2	"	"	"	2.08	"
5.	2	"	"	10	"	"	"	18.2	"	"	"	2.08	"
5.	3	"	"	15	"	"	"	18.2	"	"	"	2.08	"
6.	2	"	"	10	"	"	"	35.4	"	"	"	2.08	"
6.	3	"	"	15	"	"	"	35.4	"	"	"	2.08	"
7.	2	"	"	10	"	"	"	26.3	"	"	"	2.08	"
7.	3	"	"	15	"	"	"	26.3	"	"	"	2.08	"
8.	2	"	"	10	"	"	"	30.2	"	"	"	2.08	"
8.	3	"	"	15	"	"	"	30.2	"	"	"	2.02	"
9.	2	"	"	10	"	"	"	36.4	"	"	"	2.02	"
9.	3	"	"	15	"	"	"	36.4	"	"	"	2.08	"
10.	2	"	"	10	"	"	"	30.4	"	"	"	2.08	"
10.	3	"	"	15	"	"	"	30.4	"	"	"	2.08	"

That so many of these assays should come out so near to the actual percentage must be regarded as rather accidental and partly the result of a steady room temperature, but when it is remembered that the skill of the writer's assistant in making the measurements, is, after more than two months of almost continuous practice, much beyond that of the ordinary physician and nurse, with limited practice, a part of the unexpected accuracy is explained. That the results should be so uniform with so great a difference in the quality of the chlorinated lime, and in the quantity of the reagent taken, may fairly be credited to the method; and it shows that chlorinated lime adapted to the method is very generally accessible. Ten Cc. equal to 2 grammes of the chlorinated lime is the quantity preferred, because the action is more prompt and energetic, and sooner finished, with a more definite end reaction. No warm bath is needed, and the active shaking of bottle A is only about 4 to 5 minutes. There are two distinct reactions and these are from two to three minutes apart. The first occurs at once on the shaking together of the liquids. The shaking being continued, this first reaction abates but does not cease altogether, and soon increases suddenly to the second rush of the gas. Then the gas very suddenly ceases to go over unless the warmth of the hands shaking the bottle causes slow expansion of the gases and air in the bottle A. About four assays can be made in an hour, but about 20 minutes of this time is taken in cooling bottle A four times to room temperature in the bath.

These solutions of chlorinated lime made as described above, may be taken as the first step in making the extemporaneous solutions of chlorinated soda, also previously described. If it was known that the solutions of chlorinated lime would keep well, and if they were accessible without the trouble of being made, solutions of chlorinated soda would be entirely unnecessary. But how long the lime solutions will keep is not known, but the great probability is that they deteriorate pretty rapidly, and are not trustworthy after a month's keeping. The soda solutions, however, keep very well for many months, and if they were accessible as they formerly were, the lime solutions would be entirely unnecessary. As it is, the lime solutions may be made as above directed, and be used for a short time most conveniently, and then what is left of such solutions can be converted into soda solutions very easily, as follows:

For every gramme of chlorinated lime or 5 Cc. of the lime solution take 2 grammes of sodium carbonate, and dissolve this in 8 Cc.

of hot water by shaking in a bottle of double the capacity. To this solution add the lime solution, and shake the two well together. If the mixture gelatinizes at first set the bottle in warm water until it liquifies, and then having shaken well, pour the whole upon a paper filter. The filtrate will then be the extemporaneous solution of chlorinated soda of the U. S. P. of 1870, which will be effective in the process, and will keep well for months, or even for a year or more. Such solutions of chlorinated soda, made from the solution of chlorinated lime of the last series of trials, were used in the following series. But for a comparison of results the assays No. 1 are made from a Chlorinated Soda Solution of the U. S. P. of 1870, that is now about 1 month old.

No.												
1,	from	chlorin'd	lime	of 38 p.c.	available	chlorine,	10 Cc.	gave	2 14 p.c.	from a	2 p.c.	solution
1,	"	"	"	38 "	"	"	15 "	"	2.08 "	"	2 "	"
2,	"	"	"	26.3 p.c.	"	"	10 "	"	2.14 "	"	2 "	"
2,	"	"	"	26.3 "	"	"	15 "	"	2.08 "	"	2 "	"
3,	"	"	"	18.2 "	"	"	10 "	"	2.02 "	"	2 "	"
3,	"	"	"	18.2 "	"	"	15 "	"	2.08 "	"	2 "	"

These trials show that the range of strength in the chlorinated lime from which the chlorinated soda is made, does not affect the results so long as the variations in strength are within the limits of this set of observations, and therefore that any chlorinated lime likely to be found in the ordinary markets is as available for making solution of chlorinated soda for this process as it is for making solution of chlorinated lime for the process. In all these last trials the end reaction was slow, and therefore a warm water bath was used in every case, shortening the times of reaction to about 6 or 7 minutes, or about the same as in the use of chlorinated lime solutions.

SODIUM HYPOBROMITE AS A REAGENT.

Sodium hypobromite has for many years been used and regarded as the standard reagent for the decomposition of urea, and when well managed it leaves nothing to be desired. Its chief disadvantages are that it must be recently made, and that this requires the keeping in readiness a strong solution of caustic soda and liquid bromine, both of which are irritant and corrosive agents not free from danger when in hands not used to the management of such agents. This reagent is, however, as available for this apparatus and method as for any other, and its use has now to be described.

SOLUTION OF CAUSTIC SODA.

All authorities agree in advising 100 grammes of caustic soda dissolved in 250 Cc. of water, for this solution, and with these proportions the solution measures about 284 Cc. and has a s.g. of 1.23 at 15.6°C. = 60°F. This solution very soon cements a glass stopper in place, and soon destroys cork, so that it is best kept in bottles with rubber stoppers.

BROMINE.

Bromine is found in the markets usually in small ground stoppered vials, and these are usually rather more than half full, and are sold as one ounce each. The stopper is carefully cemented in and tied over with putty under the cover. The vials are then wrapped in paper and packed in whiting or chalk in tin cases. If the stoppers be not good, or not well put in, they will leak, and if well put in they are generally difficult to get out. But with careful warming in the flame of a spirit lamp, the fingers, or a stopper wrench will turn them. In the course of these experiments, extending over two months, eleven of these bottles have been used without loss, though not without difficulty in opening—and only one found in a leaky condition. The bromine in these weighed and measured as follows:

No.
1. Contained 32.8 grammes, which measured about 11 Cc.
2. “ 25.9 “ “ “ “ 8.5 Cc.
3. “ 28.7 “ “ “ “ 9.5 Cc.
4. “ 15.7 “ “ “ “ 5.5 Cc. leaky.
5. “ 29.0 “ “ “ “ 10.0 Cc.
6. “ 29.6 “ “ “ “ 10.3 Cc.
7. “ 29.9 “ “ “ “ 10.3 Cc.
8. “ 24.7 “ “ “ “ 8.3 Cc.
9. “ 29.1 “ “ “ “ 10.0 Cc.
10. “ 24.3 “ “ “ “ 8.3 Cc.
11. “ 30.4 “ “ “ “ 10.4 Cc.

One ounce avoirdupois is equal to 28.35 grammes, so the average is a little short. A Cc. of bromine at room temperature weighs about 2.942 grammes.

THE REAGENT FOR USE.

Authorities advise that to the above solution of caustic soda, measuring 284 Cc., 25 Cc. of bromine be added, making 309 Cc., and that the mixture be gently agitated until the bromine is dissolved. Then each Cc. of this solution will contain about 0.324 gramme of soda, and about 0.08 Cc. of bromine, equal to about 0.235 gramme of bromine. The ordinary direction for preparing the solution in small quantities is to take 10 Cc. of the soda solution, and add 1 Cc. of bromine to this, agitating gently till the bromine is dissolved. Then this quantity is all used for one assay, although greatly in excess, and it does not give as good results as smaller quantities.

This solution it is which does not keep well and, therefore, has to be freshly made, but how long it will retain its efficiency for this reaction has not hitherto been determined. To test this point approximately it was found that 1.5 Cc. of the freshly made solution was the smallest quantity that would completely decompose 2 Cc. of a 2.5 p.c. solution of pure urea. Two days later, 3 Cc. of the solution was the smallest quantity that would effect the same decomposition. Three days after the last result, 4 Cc. was required to do the same work. Seven days later, 5.5 Cc. was required. Four days later, 7 Cc. was required. Twelve days later, 8.5 Cc. was required. Nineteen days later, 13 Cc. was required. Thus, after keeping for 47 days, more than eight times the quantity was required, indicating a rate of change that is not far from 0.24 Cc. a day. But the quantities recommended to be taken for the assays are so greatly in excess of what is required, that if the recommendations be adhered to, the solution may be said to be effective for a longer time than 30 days. But it will be shown later on that too great an excess is not only useless, but appears to be hurtful. As was stated above, it was found that 1.5 Cc. of this solution when freshly made was as effective in decomposing the urea of 2 Cc. of a 2 p.c. solution of urea, as was any larger quantity, in this apparatus, and the results of the trials on this point are given below. The quantities of the solution taken were in each case made up to 10 Cc. by adding water, and each trial was repeated with the addition of 10 Cc. more of water without perceptibly varying the result.

In	No.	1	the	2 Cc. of	2 p.c.	solution	of urea	with	1	Cc.	of the solution	gave	1.51	p.c.	Failure.
"	"	2	"	"	"	"	"	"	1.5	"	"	"	1.95	"	
"	"	3	"	"	"	"	"	"	2.0	"	"	"	1.95	"	
"	"	4	"	"	"	"	"	"	2.5	"	"	"	1.95	"	
"	"	5	"	"	"	"	"	"	3.0	"	"	"	1.95	"	
"	"	6	"	"	"	"	"	"	4.0	"	"	"	1.95	"	
"	"	7	"	"	"	"	"	"	5.0	"	"	"	1.95	"	
"	"	8	"	"	"	"	"	"	6.0	"	"	"	1.89	"	
"	"	9	"	"	"	"	"	"	7.0	"	"	"	1.89	"	
"	"	10	"	"	"	"	"	"	8.0	"	"	"	1.95	"	
"	"	11	"	"	"	"	"	"	9.0	"	"	"	1.89	"	
"	"	12	"	"	"	"	"	"	10.0	"	"	"	1.89	"	
"	"	13	"	"	"	"	"	"	11.0	"	"	"	1.89	"	

These results, although fairly uniform, tend to confirm what was suspected in other trials;—namely, that too great an excess of this reagent tends to lower the result. This, if true, can only be explained by supposing that the larger quantity of solution and water present absorbs and holds a larger proportion of the nitrogen, leaving less to be measured, thus increasing this constant error so that it is noticeable by this apparatus. In a trial exactly parallel to No. 13 made with the apparatus of Prof. Doremus, for which he recommends 10 Cc. of soda solution, 1 Cc. of bromine and 10 Cc. of water for the decomposition of 1 Cc. of urine or solution of urea, the 2 p.c. solution of urea gave only 1.8 p.c. In this case exactly the same quantity of reagent and water is used for 1 Cc. of 2 p.c. solution of urea as in trial No. 13 for 2 Cc. of the same solution of urea. Everything except the proportionate quantity of urea, and therefore also of nitrogen, being the same, the one trial gives 1.8 p.c., while the other gives, practically, 1.9 p.c. The quantity of the liquid to be saturated with nitrogen, taking the same amount of the gas in each case, would probably make about this difference in the measurement of that which remained free.

Why this reagent, when thus freshly made and applied, by the same persons in the same way, does not give results as high as those obtained in the use of chlorinated lime and chlorinated soda, could not be ascertained, and the discrepancy must be charged to the imperfection of the apparatus.

THE REAGENT AS IMPROVED BY DR. RICE.

The time and trouble of preparing this solution frequently, and the risk of having it ineffective if kept, are very much lessened by a device suggested to the writer by Dr. Charles Rice, Chairman of the Committee of Final Revision of the U. S. Pharmacopœia. Dr. Rice dissolves the bromine in a solution of potassium bromide, and thus avoids the frequent handling of undiluted bromine. He uses the proportions of 125 grammes each of potassium bromide and bromine dissolved in water and made up to 1 litre or 1,000 Cc. with water, and advises equal volumes of this and the soda solution to be mixed for use near the time of making the assays. This writer assumes, for theoretical reasons, to improve the formula by substituting sodium bromide for the potassium salt, and finds it answers the purpose a little better. Dr. Rice's procedure would then be as follows :

Take the contents of an ounce vial of bromine, whatever weight it might yield, say for example, 28.35 grammes or an avoirdupois ounce, and an equal weight of sodium bromide. Having poured the bromine into a tared bottle of 500 Cc. capacity, and taken the weight of the bromine, add an equal weight of sodium bromide, and 100 Cc. of water and agitate the mixture until the bromine is dissolved. Then add water until the solution measures as many Cc. as eight times the number of grammes of bromine taken. That is, if the bromine weighed 28.35 grammes the finished solution should measure (28.35×8=) 226.8 Cc. Then equal volumes of this solution and the soda solution are mixed for the assay. This solution of bromine keeps indefinitely, so far as known, and is conveniently handled. It should be kept in bottles with glass or rubber stoppers. It contains 0.125 grammes of bromine in each Cc., and when mixed with an equal volume of the soda solution, the mixture will contain 0.0625 gramme of bromine in each Cc. It is therefore but little more than one-fourth the bromine strength of the reagent as generally recommended for this use (0.0625 against 0.235 gramme in each Cc.), yet for this reaction 5 Cc. of it are equal to 4 Cc. of the stronger solution, as is shown by the following trials. Each trial was made first with a solution in which potassium bromide was used as the solvent, and then with one in which sodium bromide was used, but as there was no practical difference in the results only those with the sodium bromide are given. In each trial the soda solution and bromine solution were mixed in equal measures, and made up to 10 Cc. with water, excepting the last one, where 5.5 Cc. of each had 10 Cc. of water added.

In No. 1. the 2 Cc. of 2 p.c solution of urea with 1 Cc. of each solution gave 0.88 p.c., Failure.
" " 2. " " " " " 1.5 " " " 1.01 " "
" " 3. " " " " " 2.0 " " " 1.57 " "
" " 4. " " " " " 2.5 " " " 2.02 "
" " 5. " " " " " 3.0 " " " 2.02 "
" " 6. " " " " " 5.5 " " " 2.02 "

In attempting to check some of the more important results of this paper by the use of the nitrometer as a more accurate instrument, it was found that the solutions of chlorinated soda were difficult to use with success because difficult to shake well, but the results obtained by the use of the other reagents were fairly confirmed by the use of the nitrometer. Even the short results obtained from the extemporaneous solution of 1 Cc. of bromine, 10 Cc. of soda solution and 10 Cc. of water for 1 Cc. of 2 p.c. urea solution,—that is, from the great excess of reagent,—were confirmed by the nitrometer, the results in two trials by nitrometer being 1.89 p.c.

ILLUSTRATION.

It now only remains to give an example of the application of the method to urine.

An adult male, in ordinary health, excreted in 24 hours 1683 Cc. or 57 fluidounces of urine. This urine was almost odorless, of good color, transparent and bright, and free from sediment when cold, of acid reaction to test paper, free from albumin when tested by heat and nitric acid, separately and together, and having a s.g. of 1.016 at 25°C.=77° F. Assayed for urea with solution of Chlorinated Soda of the U. S. P. of 1870,—first with 15 Cc. and then with 20 Cc., it gave 11.5 Cc. of displaced water in each trial. Referring this result to the first column of the Urea Table, it is found that there is no reading for half cubic centimetres, but only for 11 Cc. and 12 Cc., and therefore that the difference between 1.39 p.c. and 1.51 p.c.=0.12 p.c. has to be taken and to be divided by 2 for the half cubic centimetre, and this 0.06 p.c. has to be added to the 1.39 p.c., making the percentage for 11.5 Cc. 1.45. And this process of interpolation for the half cubic centimetre has to be applied to any other columns of the Table that are required. The observer may use either grammes or grains or both in interpreting his results, but only one is needed here to make the illustration understood. The 57 f℥. of urine is 40 f℥. from the seventh and eighth columns, plus 16 f℥. from the fifth and sixth columns, plus 1 f℥. from the third and fourth columns (40+16+1=57.), and the figures obtained by the interpolation of the "In grains" columns are for 40 f℥., 271.20 grains,—for 16 f℥., 108.48 grains,—and for 1 f℥., 6.78 grains, and these added together give 386.46 grains as the total excretion of urea for the 57 f℥. of urine in 24 hours.

On the day following, under similar conditions of diet and exercise, the same person excreted only 32 f℥. of urine in the 24 hours. The first day had been clear, sharp and cold, with high barometer, and therefore the cutaneous transpiration had been low and the kidneys had to excrete the more water. The second day was warm and clear, with falling barometer, and with winter clothing on, the cutaneous transpiration was free, so that the kidneys had less to do. The 32 f℥. of urine was of much deeper color and higher s.g. (1.022), but in all other respects was like that of the preceding day. Assayed for urea in exactly the same way it gave 18 Cc. of displaced water, indicating 2.27 p.c. of urea. Then 32 f℥. being just 2 pints, is referred to column 6 ; and, the figures in grains multiplied by 2 give 339.52 grains as the total excretion of urea in the second period of 24 hours. Then 386.46 and 339.52 added together and divided by 2 give 362.99 grains as the average excretion of urea for two successive days. This is considerably below the assumed normal, but not inconsistent with good health.

CONCLUSIONS.

The conclusions reached by the work done in this paper, may be usefully summed up as follows:

First, that the apparatus recommended is a convenient one for approximate results, and is fairly trustworthy within a total range of error of 0.3 p.c. or 0.15 p.c. on either side of the truth; and that it does not require expert skill to attain these results by its use.

Second, that the apparatus and method are not confined to any particular reagent for its best results, but may be used with any of those that have come within the scope of this paper.

Third, that the Solution of Chlorinated Soda of the U. S. P. of 1870, although not the best reagent for use, is much the most convenient, provided it can be bought ready made, simply because it is always at hand, keeps fairly well, and saves all the time and trouble of extemporaneous preparations.

Fourth, that the simple filtered solution of chlorinated lime is the best of all the reagents tried, while it gives the least trouble and requires least time in extemporaneous preparation and, the chlorinated lime from which to make it, is the most generally accessible of all the materials known to be applicable to this method.

Fifth, that the improved bromine process as used by Dr. Rice, wherein the bromine is held in permanent solution by means of sodium or potassium bromide, is much the best way of applying the bromine reagent.

Sixth, that the ordinary way of using the bromine reagent, while it is no better than other reagents, if as good, involves the most trouble and risk of all, and cannot be recommended to inexpert hands.

Seventh, that all these reagents have been hitherto used in too great excess,—not simply in wasteful excess, but also in hurtful excess.

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